University of Genova – Italian Institute of Technology

Doctoral School on "*Humanoid Technologies*":

Neuroscience, Robotics and Nanobiotechnologies

Academic Year 2006-2007

ANNEX A – V1

DESCRIPTION OF THE PhD SCHOOL RESEARCH THEMES[1]:

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[1] This is an updated version with respect to the document published before. The changes do not affect the School's research themes but clarify that this year's priority will be for the students to carry out their research at the IIT labs in Morego – Genoa.

1 INTRODUCTION

The Italian Institute of Technology (IIT) is a newly established research institution in Italy that is currently in its start-up phase. The fellowships assigned by IIT to the University of Genova are part of the start-up strategy of the Institute and have the specific goal of forming the first generation of IIT's research fellows.

To stress the multidisciplinarity of the long term goal of IIT, the fellowships offered by the University of Genova in collaboration with IIT will address aspects of the three technology platforms defined in the general scientific plan of IIT (namely: Nanobiotechnologies, Neurosciences, and Robotics).

This document illustrates the general lines of the IIT scientific plan and the start-up strategy of the doctoral program including examples of possible research topics. It is important to stress that, within the overall framework of the scientific plan, the candidates are free to propose research projects of their choice. The soundness of the project proposed will be part of the evaluation process and will be considered preferential for the choice of the individual scientific theme that will be made jointly by the tutor and the candidate.

1.1 IIT Mission[2]

As stated in the general scientific program of IIT, the

> *«merging the three platforms enables a multidisciplinary approach to robotics, in which intelligence and cognition, in combination with state-of-the-art material and nanofabrication technologies should lead to the accomplishment of a humanoid robot in the long term. The distinctive mission of IIT in its start-up phase is thus to create the forum where neuroscientists, engineers, material scientists can work together to realize the intelligent robots of the future»*.

From this standpoint, the goal is to study, design and build robots able to perform complex tasks, to learn from examples and experience, to remember and to recall from analogies, to associate past and present situations, to detect and recognize individual events and generalize from individual experiences, to predict the outcome of actions and act consequently, to explain their own behavior, to communicate in meaningful and "natural" ways, to express emotions and act socially.

This mission requires the parallel, synergic development of *bodyware* technologies in fields such as micro-mechatronics, solid state sensors, electric, hydraulic, pseudo-elastic actuators and nanoactuators, advanced materials, computational architectures, embedded systems, innovative power supply, as well as *mindware* technologies such recognition and generalization, reasoning, learning and memory, cognitive processes, artificial intelligence. It is expected that all the topics above lead to new technologies leading to artificial as well as biological materials and their interaction, the development of assembled as well as growing systems and to the study and exploitation of how function and shape co-develop in a living system[3].

Within this framework the IIT target focuses on studying, designing and building at an unprecedented level of resolution "*living intelligent systems*" in their widest sense. Scientists at IIT will not only study natural systems down to single-molecule events to transfer biological solutions into new technologies, but, more importantly, they will investigate at various levels and with different techniques the complexity and adaptability of living natural intelligent systems in an attempt to transfer this knowledge into technologies for living intelligent artifacts.

The IIT strategy can be condensed in the following three areas of activities (see figure):

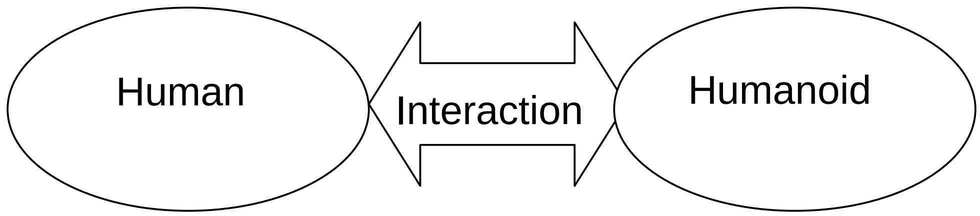
1. <u>Human Research</u> - Investigate the human "hardware" from the behavioural to the molecular/nano level. This will include: i) the link between the molecular phenotypes of individual neurons and their physiological features; ii) The genetic/epigenetic factors at the basis of learning, memory, adaptation and development; iii) The dynamics of neural plasticity.
2. <u>Humanoid Research</u> - Design and build artificial systems (humanoids) that can perceive act and learn autonomously, whilst also being able to interact with humans in a natural way (see next point). This will require the use of sophisticated materials and fabrication technologies at the nanoscale to

[2] The background material describing IIT scientific plan can be found at: http://www.iit.it/extra/contents/pdf/background_material.pdf

[3] by "living" we mean systems whose functions, morphology, computational architecture, internal knowledge, change significantly during lifetime

produce the required components (*bodyware*). Since it is unrealistic to build highly complex structures only by manipulating individual molecules, ways must be found to allow function to shape physical growth. Moreover cognitive and perceptual skills and learning abilities (just to mention a few aspects of the *mindware*), will need to be co-developed to obtain the level of intelligence targeted by next-generation humanoid systems.

3. Interaction Research - Interface these systems to humans, for example through teleoperation, tele-presence, natural language, gesture, up to the frontier of direct connection to the nervous system.



2 RESEARCH FOCUS OF ACADEMIC YEAR 2006/07 APPLICATIONS

Following the successful start-up of the doctoral school the focus of the research activities for this year's applications is on the following topics:

1. Neural Plasticity: from molecules to information coding and processing in neural networks
2. Humanoid platforms: from human learning to soft-body technologies
3. Human-machine interface: from teleoperation to direct connection

The research activities will be carried out at IIT labs in Morego (Genoa – Italy) and at the other centers of the IIT research network identified on a case-by-case basis by the School's board of professors.

The choice of the doctorate's scientific theme and of the specific laboratory will be made jointly by the board of professors and the candidate.

2.1 Neural Plasticity: from molecules to information coding and processing in neural networks

The focus of the research is the elucidation of the molecular mechanisms of neurotransmission and synaptic plasticity, starting from individual synapses to synaptic circuits up to brain diseases. In chemical synapses, which account for most if not all mammalian synapses, neurotransmitters are stored in synaptic vesicles within the presynaptic terminal and are released by a process of regulated exocytosis. Once secreted, the neurotransmitter rapidly diffuses within the narrow synaptic cleft to reach postsynaptic receptors that bind and transduce it into an electrical and/or metabolic response of the postsynaptic neuron. While neurons can rapidly transmit over long distances a digital stereotyped signal (the action potential, which cannot be modulated in amplitude, but only in frequency), a digital-to-analogic process occurs at the synapse that makes possible that an identical signal can be transmitted across the synaptic cleft in a highly modulatable fashion. The efficiency of information transfer through the synapse, called “synaptic strength” depends on the complexity of the signal transduction processes including an electrical-to-chemical transduction at the presynaptic level followed by a chemical-to-electrical/metabolic transduction at the postsynaptic level. The strength of a connection between two neurons can be either enhanced or depressed and these changes span a wide range of time windows from milliseconds to years. These mechanisms are believed to be the basis of the modifications in information flow and processing induced by epigenetic factors and eventually lead to learning and memory.

2.1.1 Neuronal and Extracellular Determinants of Network Formation and Activity

The major and most distinctive feature of the nervous system is plasticity, i.e. the astonishing ability to adapt to the environment and to improve performance over time and experience. Since the neural changes evoked by the stimuli can persist for very long times, virtually for the whole life of the individual, it seems clear that neural plasticity represents the basis of the higher brain functions such as learning and memory or, conversely, that the built-in property of neural plasticity allows experience to shape both functionally and structurally the nervous system. The first assembly of neuronal networks is driven by genetic factors, i.e. by the size of the physiological targets and the expression of chemotactic and/or cell adhesion “recognition” proteins whose genes are specifically transcribed and translated by the various neuronal populations. One of the earliest steps in the development of the central nervous system is the initiation of axon outgrowth from newborn neurons. Nascent axons navigate towards their specific targets and make synaptic connections with them, creating the intricate network found within the mature central nervous system. In doing so, the projecting axons must continuously monitor their spatial environment and accurately select the correct pathways among the various possible routes. A variety of molecular navigational systems governing axon pathfinding have now been identified. Understanding how these individual molecular axon guidance systems operate at the level of a single axon, and how these systems work in concert to initiate and steer axonal migration is a major goal in neurobiology. It has been shown that neuronal networks are capable of adaptation and learning, although a thorough study of circuit activity has been hindered by the complexity of mammalian networks. Network plasticity can be defined as the shaping of network morphology and function primarily induced by experience. This process is based on complex activity-dependent changes in neurons that modulate the ability of the neural network to transfer, elaborate and store information. We propose to clarify the mechanisms underlying synaptic transmission and plasticity in random and artificial networks of live neurons with the purpose of understanding the changes in the information flow and processing involved in higher brain functions. The investigations on the molecular basis of synaptic plasticity will include the molecular analysis of the neurotransmitter release machinery, the functional characterization of key synaptic proteins, and the map of the signal transduction and protein phosphorylation processes that mediate the changes in the efficiency of synaptic transmission. These studies will be carried out using leading edge biotechnologies, including viral-infected neuronal cell cultures, live imaging of neuronal cells coupled to patch-clamp recordings as well as generation and phenotypic characterization of genetically altered mice lacking specific neuronal proteins.

2.1.2 Network Responses to Environmental Stimuli and Network Adaptation to short- and Long-Term Plasticity Paradigms

After the first gene-driven developmental period, neuronal circuits are continuously modified and shaped by experience (epigenetic development): synaptic connections that are scarcely used become weaker and weaker and eventually disappear, whereas synapses that are heavily used become stronger and stronger and eventually increase in number. As mentioned above, synaptic strength can be finely tuned over a short-to-long time scale by a combination of factors including previous activity of the network, generation of second messengers, functional changes in pre- and postsynaptic proteins as well as regulation of the expression of genes implicated in growth, survival and synaptic transmission. This results in changes in the efficiency of synaptic transmission, that can last from fractions of seconds to minutes in case of short-term synaptic plasticity up to hours, days and months in case of long-term synaptic plasticity. These changes profoundly affect the processing between input and output information and, ultimately, shape the information flow within the network. We propose to subject random and engineered neuronal networks obtained from wild-type or genetically altered mice to chronic, spatially-defined, patterns of electrical stimulation in the presence or absence of controlled changes in the extracellular environment (ions, neurotransmitters, lipid messengers, hormones, etc). During and after the conditioning sessions, the functional and structural changes induced by experience (axon outgrowth, synapse formation, synaptic strength) will be evaluated by live imaging coupled with electrophysiology, in order to define a constellation of environmental stimuli with negative/positive influences on neural development and plasticity and capable to modify neural connectivity and information processing through the network.

2.1.3 Information Processing in Excitatory and Inhibitory Sub-Networks

Computation in neuronal networks is based on a delicate balance between excitatory and inhibitory neurons. A slight imbalance between these two components may lead to hyperexcitability and uncontrolled spread of excitation within the circuits, a mechanism that is thought to be involved in the development of epilepsy. Although excitatory and inhibitory systems share most of the main proteins involved in neurotransmitter release, they exhibit clearly distinct phenotypic traits and functional properties. As this is a topic of great interest in Neuroscience, we propose to: (i) define in detail the physiology of excitatory and inhibitory neurons in simplified circuits such as autaptic or simple microcircuits obtained through micropatterning; (ii) identify the properties of excitatory neuronal networks in which inhibitory neurons are represented to a different extent and (iii) investigate the extracellular signals (e.g., trophic factors) that, by affecting excitatory and inhibitory systems in a different fashion, alter network excitability.

2.1.4 Neuronal Targets for Therapy and CNS Diseases

Interest in neural plasticity is not limited to basic research but extends to medicine as well. Investigation in this area has already lead to significant progress, with understanding of basic brain mechanisms which are altered or defective in neurological diseases. During the last decade, knowledge of many brain diseases has grown up at astonishing rates. In particular, understanding of the affected molecular events and of their mechanisms has increased tremendously, opening the possibility to develop new therapeutical approaches. An advanced molecular and cellular investigation of adequate experimental models of neurological diseases could therefore induce significant progress in prevention, pathogenesis, early diagnosis and therapy of brain diseases. The relevance of the proposed topics to the understanding of the pathogenesis of neurological diseases is strengthened by the emerging importance of synapses and synaptic transmission as early targets of degenerative processes.

2.1.5 Set-up of Neuro-electronic Interfaces for High-Efficiency Coupling

We will develop efficient neuro-electronic interfaces which allow a bi-directional interaction between the brain and artificial devices. The research will investigate the mechanisms which allow to reliably modify synaptic connections in neuronal preparations by using the technology of multielectrode arrays and efficient coding and decoding schemes. Attention will be paid to the optimization of the cell-solid state interaction, in order to achieve long-lasting conditions of cell survival and an optimal transfer of forward and backward signals from neurons to the solid-state device. The cell culture, cell imaging and neuromorphology approaches will utilize the micropatterning facility of the nanobiotechnology platform to develop the deposition of micro dots or stripes of adhesion-proteins to achieve construction of preferential adhesion pathways along which neurons could extend their neurites. We plan to obtain targeted positioning of neuronal terminals, oriented cell motion and neurite outgrowth, which would allow us to record signals related to pathfinding and stabilization of organized contacts and networks. We have planned four complementary activities, namely: to develop new solid-state substrates favoring neuronal growth along specific pathways; to optimize cell solid-state interfacing by micropatterning of various guidance proteins; (iii) to characterize the intracellular signal transduction systems affecting cytoskeletal assembly during neuronal growth; (iv) to analyze the synaptic determinants of network formation by using genetically altered neurons; and (v) to characterize electrophysiologically neural excitability, synaptic transmission and synaptic plasticity in random and engineered neural networks. These topics will also define the framework for the development and interpretation of the neuro-electronic and neurorobotic interfaces.

2.2 Humanoid platforms: from Human Learning to Soft-body Technologies

One of the short-term goals of IIT is to develop a full-body humanoid. This objective will be pursued by addressing explicitly and in parallel the implementation of the humanoid physical bodies and the implementation of their cognitive abilities including the interface with humans in a direct and indirect way.
The overall strategy is to compare different technologies for the realization of the humanoid's bodies starting from "hard-bodied" systems already available or being developed and moving, in the years to come, toward "soft-bodied" humanoids.

In terms of functionalities the humanoid platforms (available and under development), will be used to investigate, the learning of manipulation skills and locomotion. The reference scenario will be that of a "personal helper" where not only the functions directly controlling the artificial systems are to be developed but, even more importantly, the strategies and functions supporting human-machine interaction. For example the focus will be on manipulation skills both from the "action performance" perspective (i.e. learning manipulation and object affordances) as well as "action understanding" point of view (learning to understand other's actions and to co-operate). It is worth stressing the fact that these functionalities encompass a wide range of strategic research topics such as: recognition and generalization, attention, gesture communication, affordances etc.

This research theme will offer the possibility of addressing learning with different methodologies spanning from psychophysics and brain imaging studies to implementation of cognitive artificial systems and focuses specifically on the issues of how to exploit the interaction of the humanoid with the environment in learning how to acquire multimodal information about objects. The goal of the interaction may be, for example, learning/understanding the properties and affordance of an object, the purposive use of goal-directed manipulation, the meaning of gestures and actions, how to exploit the body (self or someone else's) to communicate and how to understand communications, events, and contexts.

2.2.1 Research Platform: Bodyware

The evolution of humanoid platforms designed to collaborate with humans will be from rigid toward soft components specifically addressing technologies of skeletal, actuation and sensorial components in an integrated way. Soft-bodied robots will be based on systems where the skeletal part does not only have a support function but, coupled to elastic actuators and sensors will offer the possibility of investigating truly innovative solutions.

In relation to actuators, from the performance point of view, fundamental requirements are power/weight and power/volume performance, compliance and stiffness regulation, robustness, control behaviors and more biological issues such as self repair and tolerance to injury and adaptability during the repair process. Issues relating to the control during these repair stages will be important as the overall behavior will be modified during the healing period, and learning and updating control strategies will be essential at this time, as with a child or human. Unfortunately organic muscle is still not an engineering technology and, for the purpose of the initial implementation, the solution adopted could be based on more traditional actuators taking, whenever possible, a "soft" biomimetic approach to the actuation structure perhaps devising new mechanical configurations for available technologies (e.g. series-elastic actuators). However the fundamental technological issue of elastic actuators composed of fibers with mechanical properties similar to those of biological muscles will be investigated in depth.

The skeletal part of the body, besides providing the physical support for the sensors and actuators, represents an important functional component and a source of interesting technological solutions. In this respect we intend to investigate recent advances in material sciences opening up the possibility of using lightweight and highly flexible structures in the limbs and joints of robots. These technologies, when linked to well matched control approaches could speed-up the implementation of more human-like bodies emulating the 'soft' physically compliant structure of muscle, bone, tendons and skin.

Examples of possible research topics are:

- Design and implementation of actuators with controllable stiffness;
- Elastic actuation mechanisms and devices (e.g. elastic and pseudo-elastic actuators, shape memory alloys, pneumatic etc.).
- Haptic sensors and artificial skins (tactile arrays);
- Technologies for tendons and cabling, wiring, fabrication of the electronics, FPGA's;
- Materials with variable mechanical properties, new materials and procedures for intrinsic safety;
- Energetic considerations, study of the interaction between control strategies and power consumption, batteries.

2.2.2 Research Platform: Mindware

The mindware refers to the cognition/intelligence aspects of humanoid research and focuses specifically on the issues of how to exploit the interaction of the humanoid with the environment in learning to understand, for example, the properties and affordance of objects, the prospective use of goal-directed manipulation, the meaning of gestures and actions, how to exploit the body (self or someone else's) to communicate and how to understand communications, events, and contexts. A full integration of cognitive aspects, perception components and sensorimotor coordination behaviors is required to realize an autonomous robot. It is therefore possible to implement the mindware by taking inspiration, as much as possible, from human cognitive development, i.e. to implement cognitive skills by building a system that learns incrementally through interaction with the environment and other agents just like a human baby does.

The specific goal is to implement the *mindware* in an embodied system. Examples of specific research topics are the implementation of the following abilities in a physical humanoid system:

- Multimodal perception (e.g. visuo-tactile) and recognition;
- Active vision;
- Sensorimotor coordination (e.g. eye-hand coordination, bimanual coordination);
- Coordinated control of complex, multi degrees of freedom and redundant structures (body/hand posture and environment interaction);
- Variable impedance control strategies;
- Study, development and experimental validation of learning methods (supervised, unsupervised, reinforcement learning);
- On-line learning manipulation, affordance and tool use;
- Event recognition and generalization;
- Motivations and non-immediate rewarding exploration strategies;
- Self-organizing/adaptive modular architectures for behavior selection/generation.

2.2.3 Human Behavior and Interaction: Motor learning, multimodal Integration and human-machine interaction

The realization of intelligent machines interacting (and/or interfaced) in natural ways with humans cannot be achieved without expanding our knowledge of how humans (and to a limited extent other natural organisms) control their behaviors, learn from experience, adapt to environmental conditions and interact with each other. Conversely the implementation of artificial systems incorporating intelligent behaviors and adaptive skills typical of humans is a powerful tool to validate hypotheses and to suggest new directions of experimental neuroscience research. For example the study of motor control and learning mechanisms in humans and in animal models is important to understand how central nervous system creates and updates its internal representations, and create a vocabulary of action representation allowing great precision of movement under varying environmental conditions. To understand these mechanisms, mainly attributable to plastic changes in the cortical circuitry, represents a milestone towards understanding how the motor system can continuously adapt to the environment keeping motor precision constant. Implementing these mechanisms in humanoids might allow transferring the adaptive abilities of the human motor system to humanoid prototypes and would be a major step forward in the field.

Along this research line possible topics will be investigating human behavior by studying the relationship between motor perception and actions and the underlying brain activities.

Among the possible research topics are:

- Study of goal-directed action representation in the brain;
- Study aspects of visual attention in goal-directed manipulation;
- Study the relationship between mechanical structure and (neuro) control;
- Perception, representation and cross-modal interaction
- Brain activities underlying human-human interaction and cooperation.
- Motor control and learning (locomotion, grasping, gazing)
- Sensory-motor memory and motor learning
- Visual attention, recognition, generalization

2.3 Human-Machine Interface: from Teleoperation to Direct Connection

This activity refers specifically to the study of technologies and processes to interface artificial and biological systems and, in particular, two areas of activities: neural interfaces and tissue interfaces.

2.3.1 Neural Interface: where to connect and how

A stable, long-term recording of the activity of neurons of the central nervous system (CNS) in awake, behaving subjects is the ultimate goal. This technological challenge is shared by engineers studying how to interface prosthetic devices to the human nervous system and by neuroscientists investigating how to correlate defined sensorimotor or information-processing tasks with the functional activity of neurons. In this framework three research topics are particularly relevant:

i) to investigate the relationship between spatial location, and time evolution of brain activity and action/perception (where to connect);
ii) to investigate the technologies for micro-electrodes implementation and placement;
iii) to investigate the “communication language” used by the nervous system to code and transfer information between clusters of neurons, required for bidirectional interface between the nervous system and artificial devices.

Long term goals are both scientific, for example to understand the fundamental basis of human perception and motor representation) and technological, for example, in the field of advanced prosthesis, tele-operation and telepresence.

One general goal of this activity is to explore novel technologies to enable the recording of neural activity from the CNS over extended periods of time, with minimal invasiveness and ultimately in a highly parallel manner. Research efforts will be directed to study and implement neural interfaces on the basis of the results of biological experiments performed in conjunction and interplay with neurophysiology (particularly scientists working with non-human primates) and neurosurgery centers (those provided with experience on electrophysiological monitoring of awake patients during surgery). The specific scientific and technological of goals of these activities being that of testing the feasibility of interfacing to the nervous systems at the level of action planning and representation and through multiple, parallel connections.

The efficiency of implanted systems is directly related to the number of single neurons recorded at the same time. In this direction points the attempt to build three-dimensional arrays of recording electrodes, in some cases integrated with signal-processing electronics. These new devices do not blindly stimulate regions of the brain, but they sense their neurophysiological surroundings and utilize this information to react on demand. This could open the gate to completely new and efficient closed-loop control and therapy systems for both intrinsic (back to the brain source) and extrinsic acting (robotic output) controlled devices (bi-directionally working neuroprostheses). The concept of bi-directionality is fundamental. It is known from amputee patients, that the absence of feedback signals represents one of the major problems to achieve the sense-of-self of the prosthetic limb.

Relevant research topics are:

- Neural probes for in-vivo applications: Many issues are still open, such as the need to increase the number of electrodes, the functionalisation of the surface (better coupling for a chip-neuron interface) or to improve the spatio-temporal resolution of the probes and the reliability of the recorded signals.
- Neuro-electronic, neuro-robotic interfaces. There is a growing interest in studying advanced neuro-electronic interfaces that can be extended to neuro-robotic interfaces and that could have a big impact in the broad field of brain-machine, brain-computer interfaces (BCIs) or in the field of neuroprosthetic devices.
- Neurocomputing and Information processing in neuronal networks.

2.3.2 Tissue Interface

Interfacing biological systems to artificial devices is not limited to neural connections. Tissue engineering is one of the major focuses of biotechnological research today. The most ambitious tissue engineering schemes assume that specific tissues and organs can be restored, repaired or replaced by homologous tissues created in vitro. However, many pre-clinical and also clinical reports demonstrate that poor scaffold design and inadequate tissue culture condition are currently the major problems in tissue engineering that may prevent its successful applications. To overcome these limitations, novel biomaterials and better processes are needed.

Better designed materials are required to sustain and guide tissue regeneration. A specific area of research could seek to implement and integrate novel bio-hybrid synthetic techniques, nanotechnologies and advanced material processing technologies to obtain scaffolds able to guide and control tissue growth, differentiation and proliferation. In particular, novel materials both of synthetic and natural origin have to be designed and processed to meet specific physical, chemical, morphological and functional requirements tailored to specific applications.

Relevant research topics in this area are:

- Development of novel technologies and processes for the engineering of polymeric scaffolds, having: (a) well defined and tunable degradation rates; (b) highly structured and organized macro- and micro-porosity networks to guide cell and tissue colonisation as well as the trafficking of microsolutes; (c) specific molecular signals for cell recognition and guidance.
- Development of practical and reproducible in vitro experimental models to quantify the effects of mechanotransduction on cellular functions and on the production of ECM proteins.
- Study of the transport mechanisms that regulate fluid, macromolecular and cellular trafficking in cellular constructs, and of the experimental methods to determine the efficiency of movement of large molecules and fluids through the cellular constructs.
- Development of "smart" bioreactors for neo-tissue growth, e.g. a prototype of integrated bioreactor with feedback mechanisms, to reproduce the appropriate biological environment for tissue growth.
- Mechanical interfaces to prosthetic devices

2.3.3 Robotics for Medicine and Rehabilitation

Considering the research topics carried out in the robotics platform and the strong link between robotics and neuroscience, the area of robotics in medicine and rehabilitation is particularly interesting and strategic. Traumatic events such as limb amputation, stroke, or spinal cord injury affect, very often in a significant way, sensory and motor functions with significant effects on the person's quality of life.
Robotic systems are among the most promising technological solutions to restore some of these functions and increase the level of autonomy in at least two ways:

i) by developing advanced prosthetic devices substituting or supporting a physical loss (the so-called "home assistant systems");
ii) by developing robot-based rehabilitation devices and protocols

In the latter case, intelligent rehabilitation devices acting as a robotic physiotherapist can offer, as important advances, the ability to adapt to the individual users needs, and also the ability to follow the patient's progress during re-learning of motor skills. The kind of robotic instruments used in these cases could be: (i) exoskeletons (the robot device is supporting the limb and the human-machine interface is extended all along the limb); (ii) manipolandum (the contact between the patient and the machine is only at the end-effector).

Another important aspect to be considered is that the usability of artificial devices for functional substitution and restoration is nowadays considerably limited by the difficulty of developing effective interfaces able to restore the bi-directional link between the nervous system of the user and the end-effector to be controlled. On the other hand, recently the possibility of measuring brain activity from cortical areas is opening up new possibilities to exploit the modulation of the "shared-control" between the neural activity (i.e., the user's intention) and the low-level control for different robotic devices and different subjects.

In this respect the research carried out will be aimed at specifically developing new solutions based not only on EMG signal but also on more direct connection with the nervous system. In order to be able to effectively develop the necessary technologies basic knowledge of neural processes are essential.
For example:

- The knowledge of how the brain controls movement at the central and peripheral level is essential to inform the design of robotic interface systems to support/substitute motor and sensory abilities.
- The knowledge of what kind of proprioceptive and visual feedback is required to control movement is essential to provide the user with sufficient information through canonical and/or alternative modalities.
- A deep understanding of the mechanisms of brain plasticity, learning and memory is fundamental to stimulate in the most effective ways the re-learning of motor abilities.
- The knowledge of motor and sensory coding in the central and peripheral part of the nervous systems is essential in order to synthesize effective coding interface.

In this framework, possible research activities are the following:

- Realization of computationally-adaptive exoskeletons to support limb movements for functional substitution and rehabilitation;
- Realization of robotic devices (of the manipulandum type) supporting robot-mediated physiotherapy;
- Development of shared-control strategies driven by non invasive and invasive interfaces;
- Development of human-robot interfaces providing physical connection and neural coding translation between humans and robotic artefacts.

3 TRAINING ACTIVITIES

The multidisciplinary approach of this PhD program will attract students with different backgrounds (biology, chemistry, engineering, medical sciences, cognitive neurosciences, computer science and artificial intelligence, physics etc.). One the main objectives of this doctoral program is to give birth to a new discipline in which all these aspects can contribute to the discovery of new technologies and the implementation of new, hybrid (i.e. bionic), artificial systems.

With this aim in mind the training will start with plans tailored to the need and interests of each individual student and aimed at bringing all students to a common understanding of the key scientific aspects and investigation tools of the three IIT platforms. This will be obtained also by planning exchange of students for 6 to 12 months with laboratories where particularly interesting experimental techniques and/or strategic scientific approaches are well established. As an example, a computer scientist interested in investigating how the brain represents visuo-motor information could be trained in a neuroscience lab and engaged in behavioural or brain imaging studies. Or vice versa a student with a medical background interested in implementing an artificial or hybrid systems (e.g. a prosthetic device) will be given the possibility of acquiring design skills and tools. Hopefully starting from these diversified backgrounds students will be able to develop a common language and contribute to the establishment of new experimental procedures and technologies.