University of Genova – Italian Institute of Technology

Doctoral Course on
"*Robotics, Neuroscience, Nanotechnologies and Drug Discovery*":

Academic Year 2008-2009

ANNEX A

RESEARCH THEMES

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1   INTRODUCTION TO RESEARCH THEMES

The Italian Institute of Technology (IIT) is a research institution in Italy that is currently in an advanced 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.

Following the start of the Research Labs in the IIT's Headquarters in Genova Morego and the appointment of the first scientists, this year's research topics are proposed by the Research Directors and their senior collaborators. The candidates are asked to prepare a research project of their choice with explicit reference to the Theme proposed. The soundness of the project 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.

The themes are structured with reference to the proposing Research Directors:
1. Neuroscience and Brain Technologies (Prof. Fabio Benfenati)
2. Robotics, Brain and Cognitive Sciences (Prof. Darwin Caldwell)
3. Robotics, Brain and Cognitive Sciences (Prof. Jean-Guy Fontaine)
4. Robotics, Brain and Cognitive Sciences (Prof. Giulio Sandini)
5. Drug Discovery and Development (Prof. Daniele Piomelli)
6. Nanobiotechnologies Facility (Prof. Roberto Cingolani)

Each application must make specific reference to one of the research themes proposed.

2   NEUROSCIENCE AND BRAIN TECHNOLOGIES (PROF. FABIO BENFENATI)

Theme 2.1: Neuronal Determinants of Synaptic Transmission and Plasticity
Tutor: Dr. Andrea Barberis
N. of available positions: 1

The amplitude and the shape of the post-synaptic current are important determinants of information integration in the CNS. Their remarkable variability observed at many synapses in the CNS represents a prerequisite for a fine modulation of the network coding, plasticity and development. Despite intensive investigations, the factors underlying such variability have not been fully elucidated. The amplitude and the shape of the unitary synaptic current are believed to depend upon a number of pre- and post-synaptic factors including i) amount and time course of the agonist released in the synaptic cleft, ii) number and relative location of the post-synaptic receptors at the post-synaptic density, iii) gating properties of the post-synaptic receptors. While there is general agreement that the amplitude of the synaptic current is efficiently modulated by changing the number of post-synaptic receptors, the contribution of pre-synaptic factors remains elusive. It has been shown that, after the release of the vesicle content, the extremely brief neurotransmitter exposure makes the post-synaptic receptors be activated in conditions of strong non-equilibrium. This implies that fine changes in the synaptic neurotransmitter exposures can result in noteworthy changes of the post-synaptic response amplitude and/or duration. The aim of the research will be to understand the interaction and the relative contribution of pre- and post- synaptic factors in shaping the inhibitory and excitatory unitary post-synaptic current. The main topics that will be investigated using a combination of advanced electrophysiology and live imaging techniques are the following: (i) study of the gating properties of the post-synaptic receptors at inhibitory synapses; (ii) study of the variability of the quantal size; (iii) study of the relationship gating-mobility of post-synaptic receptors; (iv) real-time visualization of the synaptic release; (v) lateral diffusion, exocytosis and endocytosis.
For further details concerning the research project, please contact: andrea.barberis@iit.it

Theme 2.2: Neurophysiological Characterization of Mouse Models of Human Synaptopathies
Tutor: Dr. Pietro Baldelli
N. of available positions: 1

The factors that induce a neuron to maintain a correct synaptic signalling are important for understanding development of various neurological diseases. Inappropriate expression of mutated cellular molecules in the nervous system of transgenic mice is very useful for studying conditions whose pathogenesis is controversial. We plan to use mouse models of human epilepsy and mental retardation moving from the characterization of the unitary properties of the chemical synaptic transmission through patch-clamp recordings and live imaging to the neuronal network activity through microelectrode array recordings applied in cultured neurons or acute brain slices. The ectopic expression of exogenous genes in neural structures resulting from infection with retroviruses, will be also used to study the phenotypic rescue as well as the impact of mutations associated with human diseases. Our aim will be to elucidate how the functional impairment of a single synaptic protein can act as an early target of pathological processes inducing complex diseases such as epilepsy or mental retardation.
For more details concerning the project, please contact: pietro.baldelli@iit.it

Theme 2.3: Determinants of Neuronal Polarity in Vitro and in Situ
Tutor: Dr. Annette Gartner
N. of available positions: 1

The most critical initial step in the formation of neuronal networks is the establishment of proper axonal-dendritic connections, which must be temporally and spatially tightly regulated. Neurons establish a striking polarity with a single axon transmitting signals and with multiple dendrites receiving them. This neuronal polarity is the base for the establishment of proper connections in the brain and therefore my major goal will be to understand which exogenous and endogenous factors contribute to the determination of the single axon and multiple dendrites and how the site and time of axonal outgrowth is regulated. The main aim of the project is to understand at which developmental stage neurons establish their polarity in the *in situ* situation and by which extrinsic and intrinsic factors this is regulated. The polarity of neurons and their precursors is

essential for cell fate decisions, for directed migration within the cortex, and for the wiring of the brain. Thus failures in neuronal polarity establishment and migration lead to several mental diseases. The project includes studies in the development of neuronal polarity *in situ* in cortical embryonic slice cultures in order to understand how the polarity of precursors, migrating neurons and axon-extending neurons are interconnected. It will also investigate the extent to which the relevant extrinsic and intrinsic signals contribute to polarity using reductionistic models such as dissociated neurons, patterned substrates and slice overlay assays.

For more details concerning the project, please contact: Annette.Gaertner@med.kuleuven.be

Theme 2.4: Synaptic Vesicle Determinants of Synaptic Plasticity
Tutors: Drs. Silvia Giovedì, Fabio Benfenati
N. of available positions: 1

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 as well as generation and phenotypic characterization of genetically altered mice lacking specific neuronal proteins.

For further details concerning the research project, please contact: silvia.giovedi@iit.it fabio.benfenati@iit.it

Theme 2.5: Monitoring Astrocyte-to-Neuron Communication in Vivo under Physiological Conditions and in Brain Diseases
Tutor: Dr. Tommaso Fellin
N. of available positions: 1

In vitro studies have shown that astrocytes play key roles in the regulation of neuronal excitability and synaptic transmission. Astrocytes control neuronal activity by removing extracellular K^+, by reuptaking synaptically released glutamate and by releasing neuroactive molecules. By using a combination of 2-photon Ca^{2+} imaging and *in vivo* electrophysiology on transgenic mouse models, we will determine the contribution of astrocytes in the regulation of the neuronal network activity in the intact brain. Astrocytes *in vitro* release, through a process called gliotransmission, several neuroactive molecules including ATP, D-serine and glutamate. ATP, once degraded to adenosine, inhibits synaptic transmission, while glutamate, by acting on NMDA receptors, causes synchronous neuronal depolarizations. Thus astrocytes, through gliotransmission, exert a balanced excitatory and inhibitory action on the neuronal network. Using transgenic mouse models in which neurotransmitter release is selectively affected into astrocytes, we will test the hypothesis that a disruption of gliotransmission can contribute, *in vivo*, to pathological states of the nervous system characterized by an unbalance between the excitatory and inhibitory network activity such as epilepsy.

For further details concerning the research project, please contact: tommaso.fellin@iit.it

Theme 2.6: Development of Neuro-Electronic Interfaces
Tutors: Drs. Luca Berdondini, Marco Dal Maschio
N. of available positions: 1

The research will focus on two kinds of neuroelectronic interfaces: one designed for the "*in vitro*" studies on neuron networks based on multi transistor arrays and on the mechanism of photoconductive stimulation; the other for high resolution extracellular recordings and stimulation for "*in vitro*" studies and "*in vivo*" brain implantations. With the first approach, the possible applications of the photoconductive stimulation will be investigated as a "true" space-independent stimulation method for the presynaptic neuron, while simultaneously recording from the postsynaptic neuron by means of classical patch-clamp procedure. Particular interest will be focused on the possibility to implement such a stimulation method that needs a silicon substrate and the light excitation, in a custom design for a multi transistor array device in order to

obtain a light controlled neuron stimulation while monitoring many cell at the same via transistor recordings. The mechanism of photoconductive stimulation will be studied also in order to evaluate its application for the delivery of molecules of interest inside neurons by inducing a localized electroporation. On the other side, the transfer of transistor array technology from the "*in vitro*" field to the "*in vivo*" application will be studied. This kind of research will focus on the development of such technological aspects for the implantation of devices complying with: position and spatial resolution requirements of recording sites, wiring of a high number of transistors, very small device size and design of a custom readout electronic. The experience deriving from 128x128 high resolution transistor array will be considered as the starting platform for the design of this new kind of devices.

For further details concerning the research project, please contact: luca.berdondini@iit.it, marco.dalmaschio@iit.it

Theme 2.7: Mechanisms of Ictogenesis in Experimental Focal Epilepsies
Tutors: Drs. Stefano Taverna, Marco De Curtis, Fabio Benfenati
N. of available positions: 1

In experimental models, we will examine interactions within the epileptogenic areas to identify cellular, synaptic and extracellular tissue changes underlying interictal activity and seizure initiation and termination. State-of-the-art technologies will be utilized to study the morphological, electrophysiological and functional changes occurring in the epileptogenic zone. In particular imaging of voltage-sensitive dyes, molecular imaging and multielectrode arrays will be employed. Temporal lobe seizure patterns similar to those observed in humans will be reproduced in the *in vitro* isolated guinea pig brain by transient pharmacological manipulations. Intracellular recordings and multisite extracellular recordings and ion-selective (K and pH) recordings will be performed in the entorhinal cortex, subiculum and CA1 region of the hippocampus. The hypothesis that inhibition prevails at the seizure onset and is followed by synchronous hyper-excitation that promotes seizure termination will be tested. Network interactions between temporal lobe structures will be further analyzed in these models, with a particular focus on the study of ultra-slow potentials and of long-range inter-hemispheric connectivity between temporal lobe subfields in the isolated guinea pig brain. The understanding of the mechanisms of ictogenesis is crucial to develop new therapeutic strategies, in particular for those forms that are currently not cured by available treatments.

For further details concerning the research project, please contact: fabio.benfenati@iit.it, s-taverna@northwestern.edu, decurtis@istituto-besta.it

Theme 2.8: Behavioural Profiling of Genetically-Altered Mice: Relationships between Sleep and Learning
Tutors: Drs. Valter Tucci, Fabio Benfenati
N. of available positions: 1

Sleep patterns and cognitive abilities are both established during development, stabilise in adults and may deteriorate with aging. Genes play an important role in the diversity of these functions and the study of the interaction between genes, sleep and cognition is the next frontier in solving one of the major puzzling questions in neuroscience: the gap between genes and behavioural outcomes. We will work on two main projects by using the mouse as a genetic animal model: the Mus (Mice under sleep) project and the Behavioural Profiling of CNS relevant mutant lines. we will test if genetically-induced alterations of circadian rhythms are independent of the homeostasis of sleep. In addition, we will adopt efficient paradigms for extracting meaningful properties of underlying learning protocols of inbred strains and mutants. Indeed, it has been shown in humans that sleep triggers overnight learning, particularly using a motor skill finger-tapping task. The availability of animal models (e.g. in mouse genetics), which carry mutations that affect targeted traits represents a unique resource for functional studies and also provides perfect models for hypothesis-driven experiments. In collaboration with other teams at the IIT, a set of targeted behavioural and cognitive screenings will be also carried out in relevant mouse models.

For further details concerning the research project, please contact: fabio.benfenati@iit.it, v.tucci@har.mrc.ac.uk

3   ROBOTICS, BRAIN AND COGNITIVE SCIENCES (PROF. DARWIN CALDWELL)

Project proposals are grouped into four main streams: Humanoid Robotics, Biomimetics, Telepresence VR and Haptics and Medical Robotics. The themes proposed highlight this year's priorities and are to be considered as indications of the research activities planned. As such, research projects within the same areas (in addition to the outlined projects) are welcome and will be also considered.

Stream 1: Telepresence, VR and Haptics

Researchers working in this area will work on the development of multimodal telepresence and haptic interaction paradigms, and hardware/software drawing on simultaneously displayed cutaneous and kineathesic experiences, the application of these technologies in human computer interactions and human centred robotics and the key psycho-physical testing of the experiences. The work will draw on expertise in engineering (mechanical and electronic) and computer systems. There may also be a small number of opportunities for researchers from a Psycho-physics and/or Psychology background.

Theme 3.1: Bi-manual Exoskeleton for Enhanced Teleoperation and Virtual Immersion
Tutor: Dr Nikos Tsagarakis
N. of available positions: 1

The sense of touch is crucial in any kind of training or teleoperation procedures as these actions require the user to extensively engage his hand and fingers. In the recent years the rapid improvements in hardware and software to provide effective force/touch feedback has led to the development of generic haptic devices that have been applied in various training simulators and teleoperation systems. In most of these instances the mobility, dexterity and general utility for unencumbered use are relatively poor. In addition these systems provide only point contact and cannot address much more complex haptic scenarios where hands (groping with fingers or manipulation) are used to feel forces of varying levels while manipulating objects in a large workspace. To be of any advantage the touch modality should be conveyed to the user in a natural manner through a highly perceptive and transparent haptic interface.
The development of a multi degree of freedom haptic system (based on exoskeletal systems) with large isotropic working, volume, high backdrivability and multimodal feedback capability will be the core of this research. This interface will provide immersive haptic feedback involving stimulation of proprioceptive and cutaneous nerves centres to provide data on interaction force, shape, size, texture and contact pressure. The interface proposed will be composed of the following modules:

- A proprioceptive device able to measure position, orientation and force imposed by the user's arm, hand and fingers, and integrate them to feedback the contacts (position, orientation and force) under program control.
- A cutaneous display to excite the cutaneous nerves for a truly convincing realist stimulation experience during finger manipulation or groping. To stimulate these nerve endings a novel compact, lightweight device will be developed and integrated with the force feedback device.

Applicants ideally should have a background in one or more of the following fields: electronic engineering, mechanical engineering, computer science, and robotics. The candidates must have good writing and communication skills and motivation to work in a highly competitive and multidisciplinary environment.
Experience with CAD and a good knowledge of robot kinematics analysis would be a benefit but are not essential.
For further details concerning the research project, please contact: nikos.tsagarakis@iit.it

Theme 3.2: Integration of Multimodal Virtual Reality System
Tutor: Eng. Andrea Brogni, Dr. Nikos Tsagarakis
N. of Positions: 1

Virtual Reality systems are daily becoming more complex, due to the evolution of different inputs, such as motion capture, 3D sounds, bio-feedback, haptic interfaces and robots. The integration and the mode of interacting in those multi-modal environments is a fundamental area of research for this field. Different

sensory streams are coming from different devices and making an interactive application implies deal with many different formats.

The topic of the research will involve be studying the systems available in the department and the definition of a basic standard for the communications. The design and the development of a multimodal platform for the integration will be the second part of the research. The work will be based on previous studies and in collaboration with other researchers.

The ideal candidate should have a background on computer science or engineering and a strong attitude to mix theory and practice, including programming C++ libraries and interfaces for hardware.

For further details concerning the research project, please contact: Andrea.Brogni@iit.it

Theme 3.3: Interfacing a Virtual Reality Environment with Haptic Interfaces and/or Robots

Tutor: Eng. Andrea Brogni, Dr. Nick Tsagarakis
N. of Positions: 1

The sense of presence involves the human reactions during the virtual experience. How the user reacts, in behaviour, physiologically and physically, are key points for the evaluation of the level of engagement. Using haptic interfaces and robots, we will introduce other feedbacks, i.e. touch and weight or the physical presence of avatars, that will effect how the user interacts and explore how the user behaves in this configuration? What is the best paradigm for the interaction? What kind of applications would be optimal for increasing the level of presence?

The topic of the PhD will be studying the human approach in an immersive virtual environment, when a user has to deal with haptic feedback and robotics mechanism. In particular, the interaction with robotic avatars, human-like or machine, during specific collaborative tasks or experiences will be explored.

The ideal candidate should have a background on computer science or engineering and a strong attitude to mix theory and practice, including programming C++ libraries, interfaces for hardware and 3D OpenGL graphics. Experience in Virtual reality and Presence field could be an advantage.

For further details concerning the research project, please contact: Andrea.Brogni@iit.it

Theme 3.4: Investigation of the physiology and psychophysics of the human fingertip.

Tutor: Prof Darwin G Caldwell
N. of Positions: 1

The human fingers and particularly the fingertips are key to the haptic perception of contact with an environment, yet there is a comparatively poor understanding of the nature of finger tip sensing and perception.

This work will involve a study of human tactile perception using a tactile array of vertical-moving pins in contact with the fingertip. It will investigate the sensory nature of the finger tip in terms of spatial and temporal resolution, and psychophysics methodologies to evaluate human tactile performance and use this data to define and specify the design of haptic interfaces. It is also expected that the work will involve testing an use of fMRI and MRI scans.

The applicant ideally should have good background in psychophysics. Experience in robotics and graphics OpenGL is an additional bonus but not essential.

For further details concerning the research project, please contact: Darwin.Caldwell@iit.it

Theme 3.5: High Fidelity Telepresence Control of a High Dexterity robotic hand

Tutor: Prof Darwin G Caldwell
N. of Positions: 1

The teleoperation there is often a poor mapping between the actions of the operator and particularly the hand movements of the operators and the movements of the robotic end-effector. This makes high precision, high fidelity manipulation of small or delicate object exteemely difficult or impossible.

This project will bring together several research threads considering the development of high fidelity input gloves and finger tracking systems, advanced feedback systems for the fingers (hand exoskeletons, tactile array, thermal feedback) and miniature dextrous manipulators with over 23 dof and advanced tactile sensing. Applicants should have a strong engineering or physical science background.

For further details concerning the research project, please contact: Darwin.Caldwell@iit.it

<u>Stream 2: Humanoid Robotics</u>

Research in this area will focus on all areas of hardware and to a lesser extent software development for humanoid robots. The research will involve the development of novel high dexterity end-effectors that will link with the haptics/telepresence research, novel tactile sensing, the use of new structures and materials and self healing, and self repair.

Theme 3.6: Human Friendly Actuation Technologies
Tutor: Dr Nikos Tsagarakis, Dr Bram Vanderbroght
N. of available positions: 1

Robot actuation has been traditionally based on the use of heavy, stiff position/velocity and torque actuation units coupled with rigid non back-drivable transmission mechanisms. These stiff actuation groups are usually implemented by combining DC-Brushed or Brushless or AC drives with planetary or Harmonic Drive Gears and/or timing belts with a high gain PD control. These robots are optimised for precision and speed and are highly repeatable, acting within constrained and well defined environments.

Recently, with the introduction of new applications domain such as virtual/tele-presence, robot aided therapy/assistance, humanoids and personal/entertainment robotics and augmentation systems it has become increasingly clear that the traditional actuation approach is not suitable for addressing the performance requirements of these new application domains. The requirement for closer human-robot interaction have highlighted the need for robotic systems which can match the performance of biological systems in terms of ability to regulate displacements and impedance over a wide range of loads and motions enabling control of acceleration and force for enhanced performance, safe interaction and energy efficient task execution. These are key developmental features of all new generation systems. In fact, these requirements are directly linked to the actuation system. The lack of such an actuator unit that can mimic some of the properties of the natural muscle is probably one of the most significant barriers that prevented so far the development of robotic systems exhibiting bio-natural functional behaviour and performance. This limitation of the current actuation technologies is the inspiration for the research which will focus on the:

- Development of new biologically (in terms of functional behaviour) based actuation units to form the motion/force (impedance) sources for the new range of robots.
- Investigation of appropriate materials and mechanisms (fluidic and nonlinear compliant components, smart materials such Electro/Magneto-rheological fluids) to be used for the implementation of the variable stiffness, variable damping or full impedance regulation principles.
- Exploration of how these adjustable impedance principles can be embedded into the design of a conventional engineered actuator unit (electric/fluidic drives) from the mechanism point of view. To design and produce this new range of actuator groups in a compact volume without deteriorating beneficial performance attributes found on conventionally mechatronic actuators (i.e. high power to weight/volume ratio, high force to weight/volume ratio, fast response and good position and force control).
- Development of control techniques of the new range of actuation units and demonstrate their application in the development of a lower body for a humanoid robot.

Applicants for this area are should ideally possess a strong background in mechanical engineering, electrical engineering or physical system modelling and control.
For further details concerning the research project, please contact: <u>nikos.tsagarakis@iit.it</u>

Theme 3.7: Bipedal Walking for the Humanoid Robot "iCub"
Tutors: Dr Bram Vanderbroght and Dr Nikos Tsagarakis
N. available positions: 1

The humanoid robot "iCub" has been constructed within the European consortium RobotCub. The legs have 12DOF and are powered by electrical motors. In the first stage of system walking traditional control schemes will be implemented consisting of a trajectory generator and stabilizer. In the second phase stretched knee walking and the use of the toe-joint to make bigger steps will be studied. The last phase of the project consists of changing the hardware of the legs to implement compliant actuation and to adapt the control schemes to make benefit of the compliance regarding improved energy efficiency and adaptability regarding different terrains.

Applicants should ideally possess a strong background in mechanical engineering, electrical engineering, computer science or physical system modelling and control.
For further details concerning the research project, please contact: <u>bram.vanderborght@iit.it</u>

Theme 3.8: Safe manipulation using compliant actuation
Tutor: Dr Irene Sardellitti and Dr Bram Vanderbroght
N. available positions: 1

The next generation of robotic manipulators will operate out of their safety cages and in close proximity with humans. Safety hence becomes the primary concern in these devices. Passive compliant actuation is the key for safe human-robot interaction, but control schemes controlling both torque and stiffness of every actuator to combine good tracking performances under a desired safety index are still missing. A manipulator actuated with adaptable compliant actuators developed by IIT will be built. In the first stage the torque/stiffness needs to be controlled to safely track desired trajectories. In a second phase the manipulator will be controlled without the use of control elements as joysticks, but the user will directly manipulate the load which has to be sensed by the manipulator. Preferable a strategy should be developed without using sensory information from torque/force sensors.
Applicants should ideally possess a strong background in mechanical engineering, electrical engineering, computer science or physical system modelling and control.
For further details concerning the research project, please contact: irene.sardellitti@iit.it

Stream 3: Biomimetics
This area will consider the development of hardware, software and sensory systems for biological inspired robotic systems.

Theme 3.9: Bio-natural Functional Locomotion Systems and Physical Principles
Tutor: Prof Darwin G Caldwell
N. of available positions: 1

A hydraulically actuated quadruped robot (called HyQ) is currently being developed with the aim to study compact hydraulic actuation systems for legged robots and their control incorporating aspects of active/ passive joint stiffness regulation for energy efficient animal locomotion. This will including jumping and running. Furthermore the robot will serve as a platform to test compact power systems as an alternative to batteries (petrol/gas combustion engines, fuel cells, etc) to make future robots power-autonomous for several hours.
The final version of the robot will have the following estimated specifications: weight 70-80 kg (including 10kg payload), height less than 1m, four legs with three degrees of freedom each, hydraulic actuation systems, position and force sensing on joint level, compliance in joints.
The anatomical design of the legs has been inspired by the morphology of biological systems. The specifications for actuator performance result from dynamic simulations. A first prototype leg has been constructed and its performance is currently being tested.

Positions are open to work on the development of energy efficient animal-leg mechanical systems which emulate the biological systems not only from the morphology point of view but also exhibit bio-natural functional behaviour and performance. This will include the development of actuation techniques allowing this behaviour to be simulated. The ability to passively regulate the impedance of the actuator will be the key feature of the actuation units.
The first position will consider the locomotion of the robot. After studying different animal gaits such as walk, trot and gallop, dynamic simulations will test stability and efficiency of different control algorithms and motion generators. Successful control methods will finally be tested and improved on the robot platform. The second position will focus on the mechanical design of the robot (CAD), including the hydraulic actuation system, adjustable stiffness mechanisms and eventually compact power systems.

Applicants for this area are should ideally possess a strong background in electronic/electrical engineering, mechanical engineering, computer science, or a physical science.
For further details concerning the research project, please contact: Darwin.Caldwell@iit.it

Theme 3.10: Development of water hydraulic components and systems for robotics
Tutors: Dr Yang Yousheng

N. available positions: 1

Water hydraulics, which uses water instead of oil as the power transmitting medium, is environmentally friendly, non-flammable, inexpensive, clean, readily available, and easily disposable. More importantly, when compared to oil hydraulics, water hydraulics has a quicker response and a higher efficiency. In addition, it is more stable (in terms of flow velocity and efficiency) over a wide range of operating temperatures due to water's higher bulk modulus, a lower viscosity and a higher specific heat capacity. All the above mentioned advantages make water hydraulics appealing in high performance actuation techniques such as robotics.However, water (as opposed to oil) is more prone to cavitation, poor lubrication, has higher leakage and requires appropriate material and design.

The aim of the PhD project is to develop water hydraulic components and systems for robotic actuation. The position will focus on the development of compact, small size and light weight water hydraulic components, including modelling, simulation, prototyping, experiment.

The candidate should ideally have a masters degree in Mechanical Engineering or related areas. The candidates must have good writing and communication skills. Ideal candidates should have experience in fluid dynamics, and have programming skills in C or Fortran. Experience with ProE, Fluent, Adams or AMESim would be a benefit but are not essential.

For further details concerning the research project, please contact: yousheng.yang@iit.it

Theme 3.11: Autonomous Robotic Propulsion

Tutors: Dr Emanuele Guglielmino
N. available positions: 1

The aim of the project is the design of an efficient and compact propulsion system (using conventional thermal engines, fuel cells, Stirling engines, electrical motors, hybrid solutions etc) in autonomous robots. The work will focus on the integration of conventional and non-conventional engines and motors into autonomous robots (in particular on a hydraulically actuated quadruped robot, Hy-Q) using a systems engineering approach.

The candidate should ideally have a good first degree in mechanical engineering (with major in thermal engines) or an equivalent physical science.

For further details concerning the research project, please contact: emanuele.guglielmino@iit.it

Theme 3.12 Actuation and Power Systems

Tutor: Prof Darwin Caldwell
N. available positions: 1

Actuation systems, power sources and storage of energy are vital and often overlooked features of robotic and humanoid systems. Researchers working in this area will explore novel actuation technology (braided pneumatic Muscle Actuators, Polymeric actuators, Shape Memory Alloys, compliant and hybrid actuation) and the enhancement of current technologies (hydraulics, ER Fluids, MR Fluids, piezoelectric motors). The actuation systems will be incorporated into a new generation of robots having the structure, characteristics and behaviour of humans, hominoids, and/or animals.

Previous experience with these technologies would be an advantage but the programme is open to researchers with a strong background in any physical science or engineering discipline.

For further details concerning the research project, please contact: Darwin.Caldwell@iit.it

Stream 4: Medical Robotics

Theme 3.13: Integrated microfluidic devices for biomanipulations

Tutor: Dr Leonardo Mattos
No. of available positions: 1

The development of sciences such as genetics, drug discovery and environmental health has been greatly increasing the demand for biomanipulation procedures. Transgenic and gene-target animals, for example, are commonly used as models of a wide range of serious human afflictions, including diabetes, arteriosclerosis, hypertension, Alzheimer's disease, and cancer. As a consequence, the demand for efficient

and consistent biomanipulations has also increased. These are very delicate operations, which are traditionally performed on clear Petri dishes placed under a powerful microscope and using mechanical micromanipulators. The equipment employed is bulky and expensive, and the training of operators is often a very long process – up to one year for operations such as embryo microinjections. In addition, the success rate and consistency of biomanipulation procedures are highly affected by the experience and mood of the operators. Therefore, automation is highly desired in this area.

The development of novel microfluidic systems has a great potential to simplify and miniaturize the biomanipulation equipment, improve task consistency, and create a more suitable system for computer controlled operations. Hence, the topic of research will involve the identification of microfabrication techniques suitable for the construction of microfluidic devices for cell work under (or off) the microscope; the design and construction of devices for the different biomanipulation tasks; and the development of computer interfaces and controllers for the novel devices. The ideal candidate should have a background on engineering or computer science and a strong attitude towards mixing theory and practice. Experience in robotics, biological systems or real-time systems are additional bonuses.

For further details concerning the research project, please contact: leonardo.demattos@iit.it

Theme 3.14: Computer Vision for Automated Biomanipulations
Tutor: Dr Leonardo Mattos
No. of available positions: 1

The advent of high-precision motorized micromanipulators and microscopes incorporating video cameras has enabled the creation of effective teleoperated biomanipulation systems. The use of such systems has demonstrated increased consistency and efficiency of the operations, and also a significant reduction in the training time of new operators. However, these teleoperated systems still require direct control by a well-trained operator, so the biomanipulations are still susceptible to operator errors and to the inconsistency of manual operations. In addition, many biomanipulation tasks are repetitive and time consuming, so the operators spend valuable working hours performing tedious procedures. Consequently, the automation of biomanipulation procedures is highly desired.

A key element for the development of a successful automated biomanipulation system is a fast and robust vision system. Such system should be able to localize and track the objects involved in the tasks, and to provide such information as feedback to automatic controllers. Therefore, the topic of research will involve the design of accurate, robust, and fast vision algorithms for biomanipulation applications. The ideal candidate should have a background on computer science or engineering and a strong attitude towards mixing theory and practice.

For further details concerning the research project, please contact: leonardo.demattos@iit.it

Theme 3.15: Intelligent Controllers for Biomanipulation Automation
Tutor: Dr Leonardo Mattos
No. of available positions: 1

The automation of biomanipulation procedures is expected to facilitate and speedup biomedical research by improving the consistency and efficiency of the operations, and by reducing contaminations. Furthermore, automation is expected to free laboratory personnel from repetitive and tedious tasks; reduce training costs associated with the operations; and reduce the dependency of biomanipulation facilities on individual operators. However, the success of an automated system is always linked to an efficient and robust control system, which is not easily implemented for biomanipulation tasks because they are often very complex and delicate. The development of rule-based automatic controllers requires extensive process analysis and,

even then, may be susceptible to exception errors in complex tasks.

The use of machine learning and artificial intelligence techniques may offer an alternative for the development of robust and flexible control systems for biomanipulations. An interesting approach to this problem would be, for example, the development of an intelligent system that can learn tasks by observing expert operators. Another approach could be the development of simulators from which intelligent controllers can be developed. Therefore, the topic of research will involve the investigation of online or offline learning methods applied to the generation of automatic system controllers. Experimentation will be performed in collaboration with the IIT's Neuroscience Department, and will be based on the available fully teleoperated biomanipulation system. The ideal candidate should have a background on computer science or engineering and a strong attitude towards mixing theory and practice. Experience in A.I. and robotics are additional bonuses.

For further details concerning the research project, please contact: leonardo.demattos@iit.it

4   ROBOTICS, BRAIN AND COGNITIVE SCIENCES (PROF. JEAN-GUY FONTAINE)

The core of the program will deal with advanced robotics and innovations. Scientific platforms are addressing Teleoperation-Telerobotics-Virtual Reality and related technologies.

Theme 4.1: Sensory feedback in tele-operation- Analysis and optimization
Tutors: R. CHELLALI and L. BRAYDA
No of available positions: 1

Technological and conceptual advances do not enable until now to achieve full immersive tele-operation systems: one cannot address all human sensory channels and tele-operators have partial and/or distorted "images" of distant worlds. Nevertheless the human being adapts himself and perform complex remote interactions. The aim of this work is to analyze how humans correct distortions and complete the missed parts in mediated interactions (how the media is integrated within the interaction process?). This will help to shape an optimization process dealing with minimization of the ratio (Information Volume/Relevance). Consequently this will be used for both improving interfaces design and a for better understanding of human projection concept. The candidate for this PhD position will be required to have a background in computer science and electronics.
For more details please contact: ryad.chellali@iit.it

Theme 4.2: Educational mechanical looking robots
Tutors: R. CHELLALI and F. DIONNET
No of available positions: 1

Recently low cost robotics (simplified mechanical looking robots with low level autonomy) has been largely spread. Unfortunately and after the discovery phase, users and specially children abandon the "toys". Several objective and subjective factors participate to this fact (non adapted programming tools, the uncanny effect, robustness, etc…). The goal of the project is to propose new schemes and new paradigms leading to pass easily discovery-appropriation-improvement phases for educational purposes. The developments will be largely inspired by tele-operation techniques (Effectiveness of human robot interactions, simplified programming tools, …). Experiments will be conducted in educational environments to assess the proposed solutions (Edubots networks and emerging languages).
The candidates to this topic are required to have strong skills in computer science and/or science of education.
For more details please contact: ryad.chellali@iit.it

Theme 4.3: Mixed reality for collaborative frameworks
Tutors: N. MOLLET and R. CHELLALI
No of available positions: 1

We are developing a collaborative framework (Collaborative Virtual Environment) for training/learning and co-design purposes. The current system uses VR (virtual reality) technologies only. For the new CVE generation, we are targeting new functionalities such as exploitation, maintenance and dismantlement in addition to those already implemented. For this, we open the current CVE to real physical interactions through mobile vectors (for actuation and sensing) as well as adding real sensory feedbacks. The candidate for this PhD position will be required to have a background in VR and signal processing.
For more details please contact: ryad.chellali@iit.it

Theme 4.4: Advanced Algorithms and Architectures for Reasoning Systems
Tutors: Amir Fijany
No. of available positions: 1

The objective of this research effort is to develop breakthrough algorithms and highly parallel, special-purpose computing architectures for efficient and practical implementation of advanced reasoning systems, based on the Truth Maintenance Systems (TMS). A TMS is a method for representing beliefs and their dependencies, and for efficient updating of beliefs when assumptions change. Assumption-based Truth

Maintenance Systems (ATMS) represents the most complete and systematic approach to truth maintenance. Due to its unique features, an ATMS can be potentially a core element of any intelligent system that needs to handle uncertainty, inconsistency, and delays in the information it must process, or more generally for systems that must reason under changing conditions, e.g., when assumptions once valid can later be retracted. To date, however, ATMS has not been fully exploited due to the enormous computational complexity of the update operations that the ATMS is required to perform. The main objective of this research work is to explore and build upon the recent discovery of the underlying deep recursive structure of Boolean proposition lattices. This discovery leads to novel and extremely efficient algorithms that enable significant acceleration of the ATMS operations. In addition to their efficiency, these algorithms are also more complete (by removing the restrictions imposed by previous algorithms to improve efficiency) as well as extremely regular and hence they are highly suitable for massively parallel implementation on custom computing architectures such as FPGA. A combination of new algorithms, suitable for massively parallel implementation, and the computing power offered by new architectures would then enable efficient and *practical* implementation of ATMS. Such an efficient implementation could enable an entirely new classes of applications including, but not limited to, robotics reasoning and advanced control and execution, natural language processing, speech recognition, computer vision, hypothesis-exploration engines, machine discovery systems, design systems, diagnosis systems, and planners.
For more details please contact: <u>amir.fijany@iit.it</u>

Theme 4.5: Low-Power Lightweight Vision Supercomputer: Algorithms and Architectures
Tutors: Amir Fijany and Ryad Chellali
No. of available positions: 1

The objective of this research effort is to develop low-power lightweight computing architectures and associated algorithms for achieving supercomputing level capability for various embedded image processing applications. Many embedded image processing applications, such as mobile robots, Humanoid, etc., require a supercomputing level computational capability for performing various complex image processing tasks while being severely limited by the power consumption and size of the computing architecture. Emergence of new massively parallel low-power computing architectures provides a unique opportunity to achieve the goal of developing an embedded vision supercomputer with unprecedented computing capabilities. An example is the ClearSpeed CSX massively parallel SIMD architecture which offers 192 Processor Elements (PEs) with a peak computing power of about 76 GFOLPS while consuming under 20 watts. Another example is the Tilera parallel MIMD architecture which offers 64 processors with a peak computing power of 192 GOPS while consuming about 20 watts. A combination of such architectures can be envisioned as a heterogeneous (combing both SIMD and MIMD parallel computation) massively parallel architecture enabling unprecedented performance in performing both numerical and symbolic computations. However, efficient exploitation of such a computing power requires a new thinking and approach for the design of novel massively parallel algorithms for various image processing tasks. The objective of this research effort is to first conduct a survey of available low power and compact parallel architectures to choose the most appropriate for embedded image processing applications as well as the design of a heterogeneous parallel architecture. The effort will then concentrate on the design of a class of novel parallel image processing algorithms for both low- and high-level image processing tasks, that is, from various low level image filters to more complex object recognition algorithms, with emphasis on robotics applications.
For more details please contact: <u>amir.fijany@iit.it</u>

Theme 4.6: Virtual reality for human's motor-actions studies
Tutors : R. CHELLALI- T. POZZO
No. of available positions: 1

The aim of this topic is to study humans internal models of motor-actions using virtual reality technologies. VR can offer flexible immersive contexts allowing modifications of fundamental physics, mastered environments creation and many other possible scenarios. One can change for instance the gravity amplitude or direction, choose arbitrary visual frameworks, etc…
Following that, it is possible to study how human adapt motor command to achieve interaction regarding visual context's changes. This work is a joint collaboration between the Virtual Reality team and the Neurosciences team. The expected results will serve both to improve the quality of human machine interactions and to establish a better knowledge of self adaptation mechanisms.

The candidate will work on technological aspects (design and implementation of VR tools) as well as on experimental-modeling aspects (preparing, executing and interpreting trials). Good skills in computer science (programming, interactive 3D environments, IO tools, etc…) and/or experimental psychology are requested.
For more details, please contact : theirry.pozzo@iit.it or ryad.chellali@iit.it

5   ROBOTICS, BRAIN AND COGNITIVE SCIENCES (PROF. GIULIO SANDINI)

Project's proposals are grouped into three main streams: Humanoid Robotics and Cognition, Brain Machine Interface, Human Behavior and Biomechanics. The themes proposed highlight this year's priorities and are to be considered as indications of the research activities planned. As such, research projects within the same areas are welcome and will be also considered.

Stream 1: Humanoid Robotics and Cognition

The themes under this heading group the research activities targeting the humanoid platforms of the lab among which iCub (the platform of the RobotCub project www.robotcub.org) and "James" (a one-arm humanoid build to investigate manipulation and object affordance). The research themes proposed are examples of the planned activities in areas such as cognitive systems, sensorimotor coordination, advanced materials for actuation, sensing and scaffolding.

Theme 5.1: Humanoid robot tactile sensing system
Tutor: Prof. Giorgio Metta – Prof. Valle
N. available positions: 1

Tactile sensing is the process of detecting and measuring a given property of a contact event in a predetermined area and subsequent pre-processing of the signals – before sending them to higher levels for perceptual interpretation. Generally, tactile sensing is associated with the force measurement, but - in view of the above definition - the tactile sensing in robots should also include detection and measurement of object information that cannot be deciphered from the force measurement only e.g. temperature.
The Ph.D. research activity will involve the development of tactile sensing modules and hence of the skin parts for humanoid robots, their integration with robot and subsequent use in the robot control loop for exploration and manipulation tasks. The research activity will focus on a limited set of candidate transduction technologies for contact sensing; piezoelectric polymers, resistive, capacitive - being the most promising candidates for measuring geometric and mechanical quantities. The possibility of having transducers and conditioning electronics on same medium/substrate – with transducer directly coupled with an electronic device (i.e. FET/TFT device) – will be explored. While the transducers can be placed either on flexible (e.g. organic) or rigid (e.g. crystalline silicon) substrate – based on their location on the robot's body; the conditioning electronics will be implemented on the silicon substrate. Besides improving the performance of the sensing system, the approach is expected to provide a solution to wiring complexity – a key problem in robotics. Such a marriage of transducers (e.g. smart materials like piezoelectric polymers) with FET or TFT devices on rigid (e.g. silicon), or flexible (e.g. organic or elastomeric) substrates, would also improve the reliability. Sensors readout and smart processing tasks will be implemented with dedicated electronics embedded in the tactile sensing array. The networking of the modules of tactile sensing arrays, so obtained, is expected to result in a scalable system.
Applicants should have a background in one or more of the following fields: electronic engineering, microelectronics, computer science, sensors and robotics. The candidates must have good writing and communication skills and motivation to work in a highly competitive and multidisciplinary environment.
For further details concerning the research project, please contact: giorgio.metta@iit.it

Theme 5.2: Neuromorphic sensors for humanoid robots
Tutor: Dr. Chiara Bartolozzi
N. of available positions: 1

Biological sensory systems vastly outperform conventional digital systems in almost all aspects of perception tasks, where the system must process noisy and ambiguous stimuli to produce appropriate behavioral responses. Digital systems require vast amounts of resources to extract relevant information from sensors, but still fail to produce appropriate responses for interacting with the real world in real time. Part of the reason for this might be the fundamental differences in handling sensory data in biological systems and machines. "Frame-based" time sampling and quantization artifacts present in conventional sensors are particularly problematic for robust and reliable performance. On the contrary biological sensory systems make use of continuous time, stimulus-driven, asynchronous, distributed, collective, and adaptive principles, that make their interpretation of the external world reliable and robust. The goal of this project is to introduce

in the field of robotic vision the principles of biological sensory systems design. Specifically we aim at combining the design of novel data-driven biologically inspired sensory devices with the development of new asynchronous event-driven computational paradigms, with structure and morphology that are matched to the requirements of the robots body and its application domain. The candidate shall work on testing of existing asynchronous vision sensors and on the design of new sensors with non-uniform morphology, using analog real-time low-power VLSI neuromorphic circuits. The candidate will participate in the whole project development by also tackling the problem of the realization of supporting data driven asynchronous computational paradigms for machine-vision methodologies that are radically different from conventional ones, and test the developed vision system performance on advanced humanoid robotic platforms.
Requirements:
Applicants should have a strong interest in bio-inspired hardware engineering and the ability to work independently. Good skills in programming C and Matlab. Fundamental notions of microelectronics; Background in neuroscience.
For further details concerning the research project, please contact: chiara.bartolozzi@iit.it

Theme 5.3: The role of actions for perception: improving perception abilities of the humanoid iCub
Tutor: Prof. Giorgio Metta – Dr. Lorenzo Natale
N. available positions: 2

In modern robotic systems perception is too often inadequate and simplified. This seriously affects the ability of robots to cope with unpredictability and successfully interact in the real world. Artificial perception is a complex task, in which, despite great efforts in computer science, robotics and artificial intelligence, only partial successes have been achieved.
The study of perception in humans shows that the brain takes advantage of the integration of the wealth of information available from the different sensory modalities, including information about the incipient action generation. Populations of multimodal neurons are responsible on one side for controlling eye/head, arm, and grasping movements and, on the other, to interpret actions performed by others, for the recognition of objects, and to support goal-directed attention processes. The representation of the world in the brain happens through the activation of multiple pathways and involves the use of sound, vision, touch, and proprioception mixed with activations describing the current motor context and the intended goal. This requires a new way of looking at the problem of learning to extract relevant information at each stage of processing. Outstanding questions regards: How do we represent the space around us? What visual features are important? What is the relationship between sound, vision and touch? How motor information structures the recognition process? Of particular interest is the determination of the link between object-related information and the use of this information for the control of manipulation.
In this project we are interested in studying methods for improving the perceptual abilities of the humanoid robot iCub (http://www.robotcub.org), with the goal of exploring ways of using and integrating sensory information originating from the interaction between the robot and the environment. This project requires the investigation and implementation on the robot of several different elements ranging from sensory perception, to motor control, and machine learning: for example, the realization of explorative behaviors to extract information about the environment and objects. This might include grasping and manipulation, but also simpler strategies like pushing, prodding and squeezing objects. One of the goals here is to build a representation of objects that goes beyond the level of the single sensory modality (e.g. vision) but merges the visual appearance of an object with the haptic sensation it produces when grasped, or the sound it produces when touched. To reach this level of competency the robot would require the control of attention and self-recognition.
We seek candidates with a strong background in computer science and engineering, who are also interested in the study of perception and modeling of biological systems. Knowledge of electronics and mechanics is not required but it might be useful considered that the successful applicant will be working directly on a real humanoid robot.
For further details concerning the research project, please contact: giorgio.metta@iit.it – lorenzo.natale@iit.it

Stream 2: Human Behavior, Perception and Biomechanics

The themes under this heading group research activities targeting the study of how humans learn, perceive and act. This year's focus is on multimodal sensory integration, the control of redundant degree of freedom and a new topic addressing the neural correlates of biological motion inference.

Theme 5.4: Psychophysical study of unimodal perception and multimodal integration
Tutor: Monica Gori
N. Available positions: 1

In this project we will investigate the way in which unimodal sensory signals are integrated in order to obtain a robust multimodal perception of the world. As no single information-processing system can perceive optimally under all conditions, integration of multiple sources of sensory information makes perception more robust. Many recent studies have demonstrated the capacity of human observers to integrate information across various senses in a statistically optimal (sometimes termed "Bayesian") fashion, where greater weight is given to the sense carrying the more reliable information under any particular condition. Importantly, performance in the multimodal condition is always better than in either single modality. An aspect of the integration to be studied by our research group is to investigate at what age children start to integrate sensory signals, and if is this integration optimal. Another aspect to be studied is how dynamic information are integrated between different modalities, by studying the integration of visual and tactile integration of visual and tactile flow motion. One PhD student will be involved in psychophysical experiments of this research theme. The aim is to study and understand how our brain produces an integrated robust percept of the world. Backgrounds in experimental psychology, neuroscience and basic programming skills are required.
For further details concerning the research project, please contact: monica.gori@iit.it

Theme 5.5: Modular Control of Equilibrium and Movement
Tutor: Prof. Thierry Pozzo
N. available positions: 1

The program of research is based on previous results obtained during a paradigm that we developed to study both equilibrium and spatial components of a complex multijoint goal oriented task. When subjects reach targets positioned beyond arm length from the standing position, the central nervous system (CNS) has to specify the spatio-temporal characteristics of the arm movement while maintaining the whole body center of mass (CoM) within the supporting base (the feet). A number of interesting questions arise when considering together the control of equilibrium and arm trajectory formation : 1) Are the control laws governing arm movements, laid down largely using planar 2-joint tasks (and having little or no equilibrium constraints) applicable to multijoint reaching movements (requiring a high degree of equilibrium control and numerous DoF)? 2) How are equilibrium constraints integrated by the CNS during the formation of a specific end-point trajectory among a plethora of possible ones? 3) Is there a macroscopic representation (*motor primitives*) at spinal and/or supraspinal level of such components and can they be combined like building blocks to perform this task in different conditions?
Within this field of research, one PhD student will study the interaction of these two components of the action by using experimental and computational approach and modelling. A simulator based on experimental results and optimization of iterative algorithms able to find the motor solution which, respecting the anatomical and task constraints, minimizes a given cost function, will be developed. We need therefore the contribute of one PhD students possessing basic competencies in robotic, control theory or computational neurosciences.
For further details concerning the research project, please contact: thierry.pozzo@iit.it

Theme 5.6: Neural Correlates of Biological Motion Inference
Tutor: Prof. Thierry Pozzo
N. available positions: 1

The spatiotemporal discontinuity of visual input (e.g., when a person suddenly disappears behind a wall) is a common experience for human beings. Non-human primate studies (Baker et al. 2001) demonstrated that cells in the superior temporal sulcus (STS) contribute to the perceptual capacity for object permanence and support the hypothesis that the motor representation of action performed by others can be internally generated in the observer's premotor cortex, even when a visual description of the action is lacking (Umiltà et al. 2001). Recent behavioral experiments (Pozzo et al. 2006, Saunier et al. 2008), suggest an implicit motor simulation during the complete occlusion of biological motion that compensates the lack of visual input. Little is known, however, about the neurophysiological basis of the biological motion permanence and of the capability to predict the outcome of others' actions. Within this field of research, one PhD student will be involved in the development of a high density EEG system which will enable to quantify, in humans, the involvement of action representation during the perception of biological motion. The aim is to develop a high temporal resolution EEG technique to better precise the functional roles played by the STS region and by the fronto-parietal network involved in the perception of biological motion. The student will be involved both in the

recording techniques and in the online deocoding of neural signals, which will be perfomed with the aid advanced wavelet decomposition techniques to denoise the signal and information theoretic techniques to reveal the most informative components of the neural signal. The candidate should possess basic competencies in physicis, statistics, mathematics and computer science and will receive interdisciplinary training by a team composed of both experimental (Prof. Pozzo and Fadiga) and theoretical (Prof. Panzeri) neuroscientists.

For further details concerning the research project, please contact: thierry.pozzo@iit.it

Stream 3: Brain Machine Interface

The recent advancements in Neuroscience, Robotics, Microelectronics and Control Theory, make today plausible the design and the realization of artificial systems directly interfaced with the brain.

If, on one side, some artificial sensory systems, as artificial retina and cochlear implants, are more and more improving to send visual and auditory signals to the brain, few attempts have successfully been made to work in the opposite way: by extracting and decoding brain signal to drive artificial actuators. Here at IIT we are making a big effort to support a multidisciplinary project aiming at 'reading' the brain to understand and extract motor signals which may be used to control an artificial arm. The project is highly multidisciplinary and is coordinated by Pr. Luciano Fadiga. This year's focus is on fMRI from the instrumental as well as neuroscientific perspective as detailed in the following:

Theme 5.7: Machinery for functional brain analysis.

Tutor: Prof. Franco Bertora
N. of available positions: 1

There is at IIT an ongoing program to investigate the frontiers of functional MRI imaging. Any fMRI of the motor cortex has so far been performed on subjects confined in a supine/prone position in the limited volume of a traditional scanner. There are reasons to think that the analysis of subjects performing motor tasks in a more "natural" environment could produce different and more meaningful results. A study is currently in progress for an open scanner, based on an innovative magnet design, allowing functional brain analysis of a human adult in a standing or sitting position. We are looking for one PhD student with background in physics, electronics, signal processing and MRI to participate in the design of the magnet and its related equipment and to explore and conceive novel imaging techniques (MRI sequences, data acquisition modalities and image reconstruction) to be included in the development of the scanner.

For further details concerning the research project, please contact: franco.bertora@iit.it

Theme 5.8: The Neurophysiology of the Human Brain

Tutor: Dr. Elisa Molinari
N. of available positions: 1

The Phd student will use brain mapping approaches based on functional magnetic resonance imaging to investigate the structural and functional organization of cortical and subcortical motor systems.

Through this project we will better understand the functional correlates of motor planning/execution and the underlying motor circuits.

Quantitative approaches to the anatomical definition of the cortical grey matter in healthy individuals are of specific interest.

We are looking forward to one PhD student which should be competent in physics, computer science and basic neuroscience.

For further details concerning the research project, please contact: elisa.molinari@iit.it

6   DRUG DISCOVERY AND DEVELOPMENT (PROF. DANIELE PIOMELLI)

Theme 6.1: Modeling of membrane proteins
Tutor: Dr. Andrea Cavalli
N. available positions: 2

Nearly one-third of all genes in various organisms encode for membrane-associated proteins that play a fundamental role in life processes. In this respect, it is not surprising that membrane proteins also represent validated and innovative targets for the discovery of new drug candidates. Modeling of membrane proteins can provide new insights into structural features and functional mechanisms of such biological machines, and in turn open up new avenues to the discovery of small organic molecules able to modulate the biological functions regulated by these target proteins. The PhD student will use computational tools to study two main families of membrane proteins, G-protein-coupled receptors and ion channels. Homology modeling techniques (when required), molecular dynamics simulations, and molecular docking experiments will be carried out aimed at both obtaining new mechanistic insights into the members of these families, and designing new modulators for selected membrane proteins.

For further details concerning the research project, please contact: andrea.cavalli@iit.it

Theme 6.2: Design of disruptors of protein-protein interactions
Tutor: Dr. Giovanni Bottegoni – Dr. Matteo Masetti
N. available positions: 2

Interactions between proteins are at the heart of the cellular machinery, and designing molecules able to interfere with protein-protein interactions is an important challenge. However, detailed insights into the protein binding properties as well as efficient screening platforms are needed to identify small organic molecules able to disrupt interactions between proteins. In this respect, computational tools can be of a great help as they can be exploited to both disclose the molecular determinants of protein-protein interactions, and identify new chemical entities able to prevent the formation of and/or to disrupt protein-protein complexes. In detail, the PhD student will apply docking tools to predict the structure of protein-protein complexes and identify small organic molecules able to interfere with such complexes. Molecular dynamics simulations and/or metadynamics will also be used to sample the conformational space of the proteins involved in complex formation and identify conformations responsible for protein-protein interactions.

For further details concerning the research project, please contact: andrea.cavalli@iit.it

Theme 6.3: Data mining and virtual screening of compound libraries
Tutor: Dr. Walter Rocchia
N. available positions: 2

Large libraries of chemical compounds reflect the exponentially growing data-enrichment in drug discovery that trends towards fully automated solutions to study structure-activity relationships of molecules vs. their biological counterparts. The first step is the construction of databases (chemical libraries) of non-redundant compounds that can be then exploited for virtual screening experiments. In detail, the PhD student will apply computer science to construct a database of compounds either commercially or non-commercially available, which will be provided by national and international collaborators. The database will be then extended into a three-dimensional compound library containing low-energy conformations of all available molecules. All compounds will be finally screened against selected molecular targets (and/or pharmacophore models) to identify new lead candidates able to modulate the activity of a target protein.

For further details concerning the research project, please contact: andrea.cavalli@iit.it

Theme 6.4: Diversity-oriented synthesis of drug-like small organic molecules
Tutor: Dr. Tiziano Bandiera
N. available positions: 2

Diversity-oriented synthesis (DOS) is an emerging field involving the synthesis of combinatorial libraries of small organic molecules for biological screening. Several different strategies for library design and synthesis have been developed to generate libraries of compounds. A possible synthetic approach to DOS can be the use of multicomponent reactions, namely to obtain the desired product in one-pot reactions of three or more starting compounds. The PhD student will focus on synthetic approaches to complexity-generating reactions and diversity-generating processes, such as enantioselective multicomponent reactions. In this respect, the use of organocascade reactions based upon the combination of multiple asymmetric transformations in a cascade sequence provides rapid access to complex (natural-like) molecules containing multiple stereocenters in enantiomerically pure form (enantiomeric excess more than 99%) from simple precursors and in a single operation, thus matching the requirements of appropriate efficiency, scale, purity, and cost. Notably, starting precursors will be selected within the chemical space of drug-like fragments and privileged structures.
For further details concerning the research project, please contact: tiziano.bandiera@iit.it

7   NANOBIOTECHNOLOGIES FACILITY (PROF. ROBERTO CINGOLANI)

Theme 7.1: Nanocomposite materials

Tutor: Dott.ssa Athanassia Athanassiou – Prof. Roberto Cingolani
N. available positions: 4

The research in the lab involves development of nanocomposite materials combining polymers with different kinds of nanofillers.

The first kind of nanofillers are colloidal nanoparticles of different chemistry, shapes and sizes. The research deals with techniques for the optimization for the mixing and the dispersion of such colloidal nanoparticles in the polymers for the preparation of homogeneous nanocomposites samples with enhanced properties compared to the initial polymers. Depending on the nature of the nanofillers the enhanced properties can be optical, thermal, mechanical, electrical, superficial etc. Such nanocomposite samples target to a vast range of application from electronic circuits to robotics and automotive/aeronautical industries.

The second kind of dopants that will be studied are molecules responsive to external stimuli, as light, temperature, electric field, and pH. When such molecules are incorporated in polymer matrices the resulting polymeric/composite materials can change reversibly their optical, surface, electrical properties, their volume, etc. We target application such as reversible wetting of surfaces and self-cleaning processes, reversible waveguiding, microfluidics, electro-optical components such as optical switching devices, artificial muscles etc.

Apart from the development of such materials in the facility, the target of our research is also their complete characterization using scanning probe methods, optical and spectroscopic methods (including ultrafast processes), thermal, mechanical, and surface characterisation systems and optical/confocal microspopy.

Finally the research will also be involved in the processing of materials using different laser light sources. The laser sources available in the facility make available different wavelengths, power levels, and pulse durations that provide combinations that are ideal for specific processing challenges. The processing techniques will include direct formation of nanoparticles into specific sites of the polymer matrices, micro machining of materials using powerful laser that can induce ablation, and 3D photopolymerization for the preparation of 3D structures. In order to enable the full potential of laser processing to be realized, the research will also be involved with techniques for full monitoring and control of the processes.

For further details concerning the research project, please contact: athanassia.athanassiou@iit.it

Theme 7.2: Carbon nanotubes for targeted drug-delivery

Dr. Valentina Mussi, dr. Raffaella Magrassi
N. available positions: 1

Starting from their discovery in 1991, carbon nanotubes have found application in a growing number of different fields from electronics to photonics. More recently it was proposed and partially verified their possible use in the field of biomedicine, thanks to their proved biocompatibility and reduced cytotoxicity. Methods were in fact developed for attaching molecules to the outside of the hollow nanotubes opening the way both to their use as biosensors and molecular transporters. In particular, single walled carbon nanotubes (SWCNT) have shown to be able to shuttle various molecular cargos inside living cells including proteins, short peptides, and nucleic acids. This gives one the ability to target and destroy individual cells that may be cancerous or infected by a virus.

The final objective of the project will be the development of CNTs functionalized with labeling, targeting and therapeutic molecules to be used as drug delivery system, the morphological and optical characterization of SWCNT-molecules complexes, and the study of possible advanced SWCNT functionalization to improve complexes solubility and reduce residual toxicity.

To reach the further goal of applying these techniques "in vivo", also following tissue biodistribution and blood clearance rates of intravenously administered carbon nanotubes, the problem of intrinsic toxicity and correct dosage will be specifically addressed.

For further details concerning the research project, please contact: valbusa@fisica.unige.it

Theme 7.3: Polymeric nanopore devices for single molecule analysis

Dr. Valentina Mussi, dr. Elena Angeli
N. available positions: 1

Aim of the present project proposal is the fabrication of a disposable polymeric nanopore device for single molecule DNA analysis.

Nanometric holes can be produced on a thin insulating membrane separating two reservoirs of electrolytic solution containing the DNA molecules under study. If a potential difference is applied across the nanopore, an appreciable ionic current can be measured. The passage of a single molecule through the holes can then be detected as a temporary drop of the current level. By a specific chemical functionalization of nanopores on the membrane, it is possible to increase the sensitivity towards specific target sequences. These devices offer great advantages if compared to the traditional ones allowing high-throughput and low cost gene expression profiling.

Here we propose to realize a device based on the replication on polymeric materials (PDMS, COC, PMMA, PC, …) starting from silicon or metal nanopore masters. Micro and nanofabrication technologies can thus be limited to the master template production, with a dramatic reduction of the fixed costs connected with these technologies on the single final device. In this frame a Crossbeam station, where a Focused Ion Beam and a Scanning Electron Microscope can operate simultaneously, present at the Nanomed labs, appears to be the ideal tool for the realization and the complete characterization of the master on different types of substrates, as well as a full characterization of the replicas.

For further details concerning the research project, please contact: <u>valbusa@fisica.unige.it</u>

8   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.