Dottorato/PhD in
Bioingegneria e Scienze Medico-Chirurgiche / Bioengineering and Medical-Surgical Sciences

(in convenzione con Università degli Studi di Torino e il Politecnico di Torino / jointly activated by Università degli Studi di Torino and Politecnico di Torino)

XXXV ciclo

(aggiornamento del 13 giugno 2019 / update on 13th June 2019)

Elenco delle tematiche per specifiche borse di Dottorato / List of research topics bound to PhD scholarships

1) Integrated sEMG and US approach to the study of neuromechanical muscle properties. *(borsa Politecnico di Torino)*

2) Multifunctional bioactive materials with tailored properties at the nanoscale. *(borsa Politecnico di Torino)*

3) Oligomerisation inhibitors for amyloid proteins screened by molecular and multiscale modelling techniques. *(borsa Politecnico di Torino - starting grant Jack Tuszynski for 2 years, DIMEAS for year)*

4) Treatment of class 2 malocclusion using aligners. *(borsa Università degli Studi di Torino – Dipartimento di Eccellenza in "Scienze Chirurgiche")*

5) Research Towards Autonomous Robotic Microsurgery. *(borsa Università degli Studi di Torino)*

6) Modern minimally invasive endodontic outcomes. *(borsa Università degli Studi di Torino)*

7) 3D modeling in surgical assistance. *(borsa Università degli Studi di Torino)*

8) SignalOmics – Development of omics approaches for biomedical signal processing. *(borsa Politecnico di Torino)*

9) Development of scaffolds for tissue engineered in vitro models. *(borsa Politecnico di Torino – DIMEAS, azioni di incentivazione del dottorato)*

10) Novel techniques for airway replacement, with a particular interest in the development of stented vascular allograft scaffolds for airway reconstruction after tracheal and bronchial resection. *(borsa Università degli Studi di Torino – Dipartimento di Eccellenza in "Scienze Chirurgiche")*

11) Designing stimuli-sensitive biomaterials for biomedical applications. *(borsa Politecnico di Torino)*

12) Molecular Basis of Subcellular Mechanics. *(borsa Politecnico di Torino)*

13) Experimental Characterization of Biological Tissues: From The Micro to the Macro Passive and Active Physical Properties. *(borsa Politecnico di Torino)*

14) Home Care and Telemedicine. *(borsa Politecnico di Torino - DET, Azioni di incentivazione del dottorato)*

15) Biorobotics: Minimally invasive surgery in orthopaedic trauma and robots for rehabilitation. *(borsa Politecnico di Torino – Centro Polito^{BIO}Med Lab - Centro PIC4SeR - DIMEAS, azioni di incentivazione del dottorato)*

16) Microfluidic light induced 3D bioprinting: lifelike organ-on-a-chip models for drug screening. *(borsa Politecnico di Torino – Centro Interdipartimentale Polito^{BIO}Med Lab,, azioni di incentivazione del dottorato)*

PhD in Bioengineering and Medical-Surgical Sciences

cycle XXXV

(jointly activated by Università degli Studi di Torino and Politecnico di Torino)

Research Title: Integrated sEMG and US approach to the study of neuromechanical muscle properties

Funded by	Politecnico di Torino

Supervisor	Dr. Alberto Botter (alberto.botter@polito.it) Prof. Filippo Molinari (filippo.molinari@polito.it) Prof. Marco Gazzoni (marco.gazzoni@polito.it)

Contact	https://lisin.polito.it

Context of the research activity	Muscle activation and the resulting tissue displacement are traditionally studied with surface electromyograms (sEMGs) and ultrasound (US) images respectively. These two techniques are complementary in terms of measured quantity as well as of detection volume and resolution. Surface EMG detection provides a high temporal resolution on electrophysiological events occurring in the most superficial part of the muscle. Ultrasonographic devices sample images from planes broadly perpendicular to the skin, thus allowing for the detection of mechanical events in both superficial and deep muscle regions. Recently, both techniques underwent considerable advancements. By recording sEMG signals from several locations above the skin surface (high-density sEMG), it possible to describe electrical events with high spatial resolution, which allows to decompose the interferential signal in its constituent motor unit waveforms. US imaging has the potential to reveal fine spatial details of tissue displacement, and recently such spatial resolution is beginning to be complemented by increasing temporal resolution (>1,000 frames/s), enabling in vivo estimation of the mechanical properties of activated fiber bundles in localized muscle regions. Combining sEMG and US has therefore the potential to provide key insights into the electromechanical properties of skeletal muscles, i.e. a detailed description of muscle function, from the neural excitation to the resulting muscle tissue displacement. This approach can contribute to the study of muscle physiology/pathophysiology, to the refinement of musculoskeletal models, to the assessment of rehabilitation outcomes, and to the adaptations due to ageing, pathologies or injuries.

Objectives	The candidate will be required to: • Develop and validate an appropriate electrode technology to record sEMG and US from the same muscle region minimizing any mutual interferences. • Develop multi-modal approaches for the information extraction from simultaneously-recorded sEMG signals and US images. • Test the developed technology to applied context The candidate will be involved in the following projects: • Identification of fasciculation potentials in ALS patients through a combined sEMG-US approach. • Study of neuromechanical adaptations to rehabilitation and training • Quantification of the healing process of muscle lesions

Skills and competencies for the development of the activity	The candidate should have a background in biomedical instrumentation, signal processing and interpretation. It is required a documented expertise in the analysis of physiological data, especially US images and HD-sEMG signals during voluntary and electrically-induced contractions. Good knowledge of the acquisition instrumentation and skills in the management of an experimental protocol including the integration of several devices is also necessary.

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Research Title:
Multifunctional bioactive materials with tailored properties at the nanoscale

Funded by	Politecnico di Torino

Supervisor	Prof. Enrica Verné enrica.verne@polito.it Prof. Marta Miola marta.miola@polito.it

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Context of the research activity	Several inorganic materials, such as some silicate glasses, glass-ceramics and calcium phosphates, have been shown to be bioactive and resorbable and to exhibit appropriate properties which make them suitable for bone and soft tissue engineering applications. However, the precise mechanism of interaction between such inorganic materials and human cells are not fully understood, which has encouraged considerable research work in the biomaterials community during the last decade. Particularly, recent advances have been reported in fabricating biomaterials doped with trace elements (e.g. Fe, Zn, Sr, Mg, Ag and Cu) and investigations on the effect of these elements on the biomaterial biological performances (i.e. osteogenesis, angiogenesis and therapeutic effects such as antibacterial, antioxidant, antitumoral, wound heling properties) are object of several papers. The biological response to artificial materials depends on many parameters such as chemical composition, topography, porosity and grain size.

Objectives	Many trace elements at different oxidation states can be added in glasses both as network former, modifier, as well as metal or oxide nanoparticles. Focusing the attention on biomedical applications,

	many elements has been included in the composition of several bioactive glasses and glass-ceramics, a class of materials widely studied as bone and soft tissues substitutes for their ability to chemically bond to living tissues through a peculiar surface reactivity, which implicates ion-exchange between glass and biological fluids, and the development of a reaction layer with affinity with connective tissue. Silica-based bioactive glasses and glass-ceramics doped with several trace elements can been obtained by sol–gel, as well as by the traditional melt and quenching technique. These materials can be also enriched with therapeutic chemicals by in situ reduction of nanoparticles, surface functionalization, and can be designed to be used as bulk, scaffolds, coatings, micro- or nano-sized powders as dispersed phase in organic matrices or injectable carriers. In the present project, silica-based bioactive glasses, prepared by melt and quenching route or by wet chemistry, will be tailored and modified in order to develop multifunctional biomaterials, with the aim of combining their bioactive properties with therapeutic actions, such as antioxidant, angiogenetic, antitumoral or antibacterial properties, depending on the final use destination. These properties will be achieved by physical and chemical treatments or by surface tailoring, in order to induce the enrichment of trace elements, metal nanoparticles or organic chemicals with therapeutic effects.

Skills and competencies for the development of the activity	Basic skills in materials science and technology, biomaterials/materials for bioengineering, bionanotechnology. Familiarity with the main methodologies of materials synthesis and investigation of biocompatibility, bioactivity, as well as chemical, physical and mechanical characterization of materials. Ability to translate theoretical aspects into biologically-relevant implications for the design, realization and characterization of materials for biomedical applications. Skills on critical revision of reference literature. Team-working ability.

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Oligomerisation inhibitors for amyloid proteins screened by molecular and multiscale modelling techniques

Funded by	Politecnico di Torino - Starting grant Jack Tuszynski (2 years), DIMEAS (1 year)

Supervisor	Prof. Jack Tuszynski, Prof. Marco A. Deriu

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Context of the research activity	Nowadays, progressive diseases and disabilities have a strong impact on the quality of life and cost of healthcare in the aging population. Improve the physical, social and mental well-being of this population remains one of the main current challenges. In this context, irreversible neurodegenerative disorders. The common underlying mechanism of neurodegenerative processes is a pathological protein misfolding and aggregation. Neurodegenerative diseases are in general characterized by misfolding and aggregation of amyloid proteins. In the past, several experimental researches focused on investigation and characterization of amyloid assemblies. Nevertheless, more recently also computational modelling was considered to investigate molecular features leading to aggregation in several neurodegenerative disorders such as Parkinson's, Ataxia, Alzheimer diseases. However, molecular mechanisms driving to aggregation are still debated and a deeper understanding between protein misfolding and aggregation, in particular in presence of a binder may help toward a better rational design/optimization of effective inhibitors.

Objectives	Taking advantage of molecular modelling techniques, the research is oriented toward a better understanding of the relationship between misfolded protein structure and polymorphism of oligomerization (e.g., beta amyloids). This research ultimately aims at providing new modelling approaches to design disease-

	modifying therapeutics to inhibit amyloid oligomerisation. O1: REFINE EXISTING IN-SILICO OLIGOMER MODEL. We will start from existing models of beta amyloid and alpha synuclein oligomers. Classical and enhanced sampling molecular dynamics will allow to obtain a set of disordered assemblies. Structural fluctuations will be investigated by means of molecular dynamics simulations constrained by experimental data to identify most likely conformations of oligomers to be further employed. O2: DEVELOP A PHARMACOFORE MODEL ABLE TO BIND SEVERAL OLIGOMER CONFORMATIONS. We will employ a structure based approach to define a pharmacophore models using several different oligomer conformations as protein templates. Then we will merge pharmacophore features in one single drug model to screen among compounds contained in database such as ZINC, CHEMBL, etc.. O3: ELUCIDATE PHARMACOLOGICAL COMPOUND EFFECTS ON MONOMERIC AND OLIGOMERIC CONFORMATIONS. Hit compounds (few compounds are expected to match shared features among pharmacophore models described) will be further screened by all-atom classical and enhanced sampling approaches able to deeply investigate the ligand effect on protein aggregates. Local and global effects related to ligand-target interactions will be elucidated at a single molecule level. A comprehensive datasets detailing the relationship between protein-ligand interaction and protein conformational arrangement (i.e., exposure of hydrophobic patches, secondary structure changes, gyration radius) will be generated. In more detail the free energy landscape will be quantified as a function of specific collective variables such as experimental chemical shifts, secondary structure, hydrophobic contacts, and gyration radius or a composition of them. The proposed computational activity will shed light on biophysical properties of monomeric conformation and assembly features. Ligand-protein interaction investigation will also allow to highlight ligand moieties important to increase affinity and efficacy of the ligand. This should reveal commonalities and divergences in their action mechanisms.

Skills and competencies for the development of the activity	We are looking for talented and motivated candidates with a Master Degree in Biomedical Engineering and with previous experience in the fields of molecular modelling with focus on atomistic and coarse grained molecular dynamics, enhanced sampling, dimensionality reduction techniques, data clustering, docking calculations, characterization of ligand affinity, intra- and extra-cellular kinetics.

	The candidate should also have high confidence with Linux environment and ability to deal with HPC clusters, such as CINECA. The candidate should possess a good knowledge of English Language in both written and oral forms.

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(jointly activated by Università degli Studi di Torino and Politecnico di Torino)

Research Title: Treatment of class 2 malocclusion using aligners

Funded by	Università degli Studi di Torino - Dipartimento di Eccellenza in "Scienze Chirurgiche"

Supervisor	Prof. Elio Berutti Dr. Andrea Deregibus Dr. Tommaso Castroflorio

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Context of the research activity	In the field of orthodontic therapeutic instruments, transparent aligners have been much improved in the last 20 years, their use has been studied for a long time, and the used protocols increased. One of the most important malocclusion is the Class 2 Division 1 with hypomandibolia. In case of a patient intercepted during the period of adolescent growing peak, the therapy for this malocclusion involves the use of devices that stimulate the mandibular growth. Studies by Rabie et Al have shown that, during the growth period, appropriate stimuli at condylar level can increase the amount of mandibular growth. A few years ago, starting from these concepts, a manufacturer of aligners has included the possibility of obtaining this stimulus through an appropriate mandibular advancement. The clinical validity of this tool is certain today, but the results of this stimulation at the cranial / cephalometric level has not been studied.

Objectives	The aim of the research is to assess whether and how much is

	possible to increase the mandibular growth in patients with malocclusion of Class II division 1 with hypomandibolia, treated with aligners provided with mandibular advancement. The selected subjects must be in a CS3 growth stage according to the classification of Franchi et Al to maximize the possibility of jaw growth stimulus. The results will be evaluated from a cephalometric point of view with two teleradiographies taken one at T0 before the beginning of the therapy, and the second when the results are obtained, however not before 18 months from the first teleradiography. As control group, the cranial growth data published by the Ann Arbor Cranial Growth Center will be used.

Skills and competencies for the development of the activity	Expert orthodontist with certified experience in the diagnosis and treatment of malocclusions using aligners. Experience using functional appliances.

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Research Towards Autonomous Robotic Microsurgery

Funded by	Università degli Studi di Torino – borsa di Ateneo

Supervisor	Prof. Mario Morino Prof. Alberto Arezzo Prof. Fabrizio Rebecchi

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Context of the research activity	After more than a decade since the introduction of surgical robotics in hospitals, the field is now flourishing with skyrocketing investments from leading technology and medical firms. While the main focus of commercial companies remains teleoperated platforms for minimally invasive surgery, there are unmet clinical and technological needs in providing robotic solutions to automate surgical tasks in microsurgery. The TAuRoS H2020 project stems from a concerted effort of robotics researchers, engineers and surgeons towards the development of a surgical robotic system that integrates new multimodal sensing capabilities and a novel surgery automation paradigm into a robotic microsurgery platform with advanced mechatronics design.

Objectives	The three unique technological pillars of TAuRoS are (1) using TeraHertz and hyperspectral imaging in surgical robotics to enable reliable feature extraction for automation of surgical tasks and to sense physiological information that is crucial for functional tissue characterization, (2) an innovative semi-autonomous control strategy that will allow the surgeon to operate in less stressed conditions while guaranteeing safe and robust execution of surgical procedures, (3) an open research platform based on Pico, the first microsurgical robotic platform developed by our industrial partner which will be on the market in Spring 2020. Three different clinical scenarios involving vessel anastomosis, nerve anastomosis, and transanal surgery have been identified by our surgical team to develop and test new robot-aided surgical procedures. The work plan will generate exploitable results to be directly integrated into future releases of the Pico

	platform, thus accelerating both the time-to-market and the beneficial impact on patients resulting from increased availability of microsurgery. In summary, TAuRoS is committed to enabling automation of surgical tasks via multimodal sensing and expanding the reach of microsurgery via an innovative robotic approach.

Skills and competencies for the development of the activity	The charatetistics of a successful candidate are: • Expertise in General surgery with specific competence in gastroesophageal and rectal cancer; • Expertise in mininvasive surgery; • Expertise in robotic surgical technology; • Proactive approach to join a three-years research program and carry out interdisciplinary research.

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(jointly activated by Università degli Studi di Torino and Politecnico di Torino)

Research Title: Modern minimally invasive endodontic outcomes

Funded by	Università degli Studi di Torino – borsa di Ateneo

Supervisor	Prof. Elio Berutti Prof. Damiano Pasqualini Dr. Mario Alovisi

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Context of the research activity	Endodontic therapy is a conservative treatment modality yielding a long-term retention of teeth with pulpal or periradicular disease (Salehrabi & Rotstein, 2010). The success of the endodontic treatment depends on an appropriate shaping with respect to the original root canal anatomy (Schilder 1994, Peters 2004). The canal scouting with stainless steel sizes 08–10 K-files provides the initial patency and the tactile feedback (Burklein & Schafer 2013). The subsequent glide path phase reduces the risk of taper lock and torsional stress of the shaping instruments (Peters 2004, Berutti *et al.* 2004). The root canal shaping optimizes disinfection and facilitates the tridimensional obturation (Peters 2004, Metzger *et al.* 2013, Hulsmann *et al.* 2005). The glide path and shaping techniques require the use of manual or mechanical nickel-titanium (NiTi) instruments. The latter can be classified according to the type of movement performed: rotary or reciprocating (Haapasalo & Shen 2013, Grande *et al.* 2015). NiTi rotary and reciprocating instruments reduce shaping time, operator fatigue and the risk of canal transportation, compared to manual ones (Grande *et al.* 2015, Gambill *et al.* 1996, Alovisi *et al.* 2016). Modern NiTi shaping instruments' features influence the quality of the endodontic treatment affecting the long-term tooth prognosis. The new design and alloy properties aim to improve the cyclic fatigue resistance, the root canal shaping ability and the removal of dentin debris (Adıgüzel &

	Capar 2017, Özyürek *et al.* 2017). The efficiency of the shaping instruments is related also to post-operative patients' quality of life (QoL) (Iqbal & Kim 2008). The effect of oral health problems on QoL comprises chewing ability, communication with others and appearance (Hamasha & Hatiwsh 2013). Patient satisfaction is one of major issues in dental care delivery. Therefore QoL evaluation following any dental treatment should be taken into consideration by the clinician through the use of self-assessing questionnaires (Dugas et al. 2002).

Objectives	In recent years the concepts of assessing and reporting the outcomes of health care, including dentistry, have evolved in the search for evidence base to support treatment procedures (Anderson 2000). Preoperative status combined with treatment techniques and clinician's experience may significantly influence postoperative outcomes (Pasqualini et al. 2012). In particular, the size and the taper of the instrumented canals, as well as the shaping ability of the endodontic instruments may affect the tooth prognosis. Radiographic and clinical criteria are usually used for a dichotomized outcome (Friedman et al. 2003). Periapical tissues are classified as "healed" in the absence of (a) radiographic signs of apical periodontitis (PAI score < 3) (Orstavik et al 1986), and (b) clinical signs and symptoms other than tenderness to percussion. For descriptive purposes, all asymptomatic teeth are considered to be "functional" regardless of the PAI score. The objective of the present research is the evaluation of the long-term teeth prognosis after shaping with different NiTi instruments and the influence of the endodontic treatment on the post-operative patients QoL. Moreover the impact of the modern rotary and reciprocating files shaping techniques on immediate postoperative patients' QoL was analyzed through a OHIP questionnaire.

Skills and competencies for the development of the activity	Expert endodontist with certified experience in the diagnosis and treatment of teeth affected by pulpitis, pulp necrosis and apical periodontitis. The ability in the use of the modern NiTi shaping instruments is also requested.

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(jointly activated by Università degli Studi di Torino and Politecnico di Torino)

Research Title: 3D MODELING IN SURGICAL ASSISTANCE

Funded by	Università degli Studi di Torino – borsa di Ateneo

Supervisor	Guglielmo Ramieri (guglielmo.ramieri@unito.it) Enrico Vezzetti (enrico.vezzetti@polito.it)

Contact	Includere website del gruppo di ricerca, in modo che il potenziale candidato possa accedere ad altre info

Context of the research activity	3D digital technologies were introduce in medicine in the 90', but it is only in the last decade that they have really improved surgical procedures. Computer-aided surgical planning, customized implants and intraoperative tools have demonstrated efficacy in oncology, reconstruction, post-traumatic and malformative repair, especially in cranio-maxillofacial and orthopedic surgery. A number od industrial companies offer digitalized solutions and customized products, but the production time, cost and limited flexibility of the industrial procedures penalizes the potential development and diffusion of these technologies. The University and Polytechnic of Turin have realized previous researches which allowed to acquire experience and know-how in 3D modeling for medical application, digital surgical planning and rapid prototyping, and to validate their application in clinical series. Excellent results were obtained in maxillofacial applications in terms of reduced surgical invasiveness, increased flexibility, sustainability, which suggests the possible extension to use in orthopedic, cardiovascular, thoracic and abdominal surgery.

Objectives	The research aims at the development and validation of new digital solutions which include 1) surgical planning and 3D printing for new applications, 2) improved flexibility and customization, 3) modeling of soft tissue parts in anatomical models and simulators for surgical training, 2) digital production of customized implants suitable for regenerative procedures. Specific objectives are the acquisition of the knowledge and techniques for an "in-hospital" workflow, and the development of a team approach joining surgical and engineering competency in the clinical set-up.

Skills and competencies for the development of the activity	- Industrial Engineering or Industrial Design degree; - Experience in solid modeling of medical data (CT, MRI); - Experience in CAD, 3D statistics, 3D printing and additive manufacturing;

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(jointly activated by Università degli Studi di Torino and Politecnico di Torino)

Research Title: SignalOmics – Development of -omics approaches for biomedical signal processing

Funded by	Politecnico di Torino

Supervisor	Prof. Filippo Molinari (filippo.molinari@polito.it) Prof. Marco Knaflitz (marco.knaflitz@polito.it)

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Context of the research activity	In the last three years, Machine Learning (ML) has had a tremendous impact in the field of data processing and classification. The possibility of extracting information from very large and heterogeneous data sets in a fast and accurate way has opened completely new research topics. In the field of biomedical signal and image processing, ML has usually been declined as an implementation of "-omics" analysis: large databases have been merged to clinical data and fused with previous technical experiences and processing strategies, in order to construct a huge set of descriptors (or features) to be fed to the ML systems. One of the most prominent topics in this field is "radiomics", which denotes a process where a very large set of features are extracted from medical images and then fed into convolutional neural networks (CCNs) in order to get an output (either segmentation, or classification, or interpretation of the image content). Features can be of any kind, from basic intensity or shape models, to the most advanced and subtle texture descriptors. Currently, radiomics approaches have been proposed in different important fields, ranging from cancer research, to cardiology, to image retrieval in large databases. Despite the limitations still affecting radiomics methods (the two most relevant being the difficulty of extracting so many features and the impossibility to actually optimize CNNs with limited number of data), the lesson learned from these researches is that information is hidden in several aspects of the image itself. "-omics" approaches in the field of signal processing are still not fully

	developed, nor consolidated. Recurrent neural networks (RNNs) have been proposed for the analysis of biomedical signals, but there is still a lack of methodological agreement on how to perform the feature extraction and from which domain. This because signals, unlike images, often require multi-modal analyses combining time, frequency, time-frequency and also non-linear processing. Hence, the overall topic of this PhD research program is the development of "SignalOmics" methods, mainly in the field of neurology, neurovascular assessment, and cardiology.

Objectives	The candidate will be required to: • Develop innovative methods for the feature extraction from biomedical signals. • Develop innovative methods for signal decomposition and analysis, by surpassing the current limitations of traditional decomposition methods (like empirical mode decomposition, or wavelets). • Participate to clinical studies and campaigns of data collections in collaboration with clinicians. The candidate will be involved in the following projects: • Assessment of the neuro-cognitive performance from EEG signals and physiological correlates. • Innovative signal processing algorithms for pulse-wave velocity estimation. • Assessment of the effect of central nervous performance on peripheral vascularization. It is expected that, at the end of the PhD activity, the candidate will be able to propose a unified framework for the signal analysis in a "-omics" environment.

Skills and competencies for the development of the activity	The successful candidate has a strong and documented expertise in at least two of these topics: - EEG signal analysis - ECG signal analysis - NIRS signal analysis - Vascular/cerebrovascular assessment and should demonstrate the knowledge of traditional analysis methods (time, frequency, and time-frequency approaches) and of non-linear methods (i.e. complexity analysis, empirical mode decomposition, etc …). Programming skills and experiences in the implementation of CNNs/RNNs in MATLAB language are appreciated.

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Research Title:

DEVELOPMENT OF SCAFFOLDS FOR TISSUE ENGINEERED IN VITRO MODELS

Funded by	Politecnico di Torino – DIMEAS, azioni di incentivazione del dottorato

Supervisor	Gianluca Ciardelli, gianluca.ciardelli@polito.it (POLITO) Valeria Chiono, valeria.chiono@polito.it (POLITO)

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Context of the research activity	Tissue engineering/regenerative medicine (TERM) aims to the design of functional three-dimensional constructs with the potential to restore, maintain or improve the functionality of damaged tissues or whole organs. In a recently emerging approach, TERM principles are being explored to develop 3D tissue/organ models, which could work as useful tools to (i) screen among newly designed therapeutics (free drugs or drugs encapsulated in nano/micro carriers), (ii) set-up and optimize patient-specific therapeutic protocols, and (iii) thoroughly elucidate fundamental aspects of cell functions. Bioengineered models can be designed to recapitulate in vitro the native human environment at different degrees of aging, in healthy and pathological conditions, thus allowing the investigation of aging and pathology effects on tissue/organ functionality as well as the identification of the mechanisms involved in aging processes and disease onset and

	progression. The research activity will be aimed at the development of tissue-engineered *in vitro* models of cancer and ischemic heart disease, as they represent the two main causes of mortality worldwide. Heart failure (HF) is a global pandemic affecting more than 26 million people worldwide and increasing in prevalence due to progressive ageing of population. On the other hand, there were 9.6 million deaths from cancer worldwide in 2018. The four most common causes of cancer death have been lung, bowel (including anus), stomach and liver cancers, accounting for 44% of all deaths. In this scenario, engineered models of pathological human tissues (affected by cancer or mimicking post-infarct cardiac scar) represent key tools to investigate new therapeutic options in reliable and predictive models. Importantly, this kind of research is aimed at reducing, refining and replacing the use of animals in the research (3Rs principle). The newly adopted EU Directive on the protection of animals used for scientific purposes requires that EU members increase their collaboration to follow 3Rs principle. In this scenario, this Ph.D grant represents one important first initiative of Politecnico di Torino as a member of the Italia 3R Center. For in vitro tissue modelling, the proper design of 3D matrixes that provide the structural and mechanical support to cell homing, growth and organization is a key aspect to stimulate and control the formation of a new functional tissue as well as to guide the differentiation of stem cells. By mimicking nature, the optimal 3D scaffolds should finely replicate in vitro the physico-chemical and mechanical properties as well as the porous structure of the extracellular matrix (ECM) of the native tissue, at different degrees of aging, in healthy or pathological conditions. Moreover, the degradation of the scaffold should match the rate of the specific tissue growth, without releasing toxic products. In order to design scaffolds with these properties, the selection of the raw material and the scaffolding technology is a crucial issue to be addressed. This Ph.D. program is thus focused on the design and optimization of new polymeric biomaterials (of synthetic, natural or bioartificial origin) to be used as forming materials in the development of 3D scaffolds as well as micro/nano-carriers to be applied in TERM, nanomedicine and advanced therapies. The developed strategies are expected to significantly advance the biomedical field, contributing to the definition of a new material/technology platform, which, in principle, could answer to the specific need of researchers, patients, surgeons and medical doctors. The research will also contribute to get new insights into impactful diseases such as cancer and coronary heart disease.

Objectives	The Ph.D. student will be responsible for:

	(i) the design and characterization of new polymeric materials (ii) the processing of the newly developed biomaterials into 3D constructs via additive manufacturing techniques, electrospinning and micro/nano- particles for localized and prolonged drug release (iv) the surface functionalization of the designed constructs with decoration moieties for active targeting of the developed particles and the mimesis of the native environment from a biochemical point of view. More in detail, the Ph.D. student will develop and validate bioengineered tissue models and will test on them newly designed therapeutics. These final goals will be achieved through a bottom-up approach encompassing the following steps: (i) the design and characterization of new polymeric materials of natural, synthetic or bioartificial origin, with the aim to create a library of different compositions with a wide range of physico-chemical properties (e.g. mechanical properties, degradation kinetics), with the potential to meet the properties of different tissues of the human body; (ii) the microfabrication of the optimized polymeric biomaterials via advanced fabrication technologies (e.g. melt- and solution-electrospinning, bioprinting, fused deposition modeling) into 3D scaffolds that in vitro recapitulate targeted human tissues at different stages of ageing and/or pathology progression; (iii) the surface or bulk functionalization of the designed constructs with proteins or peptide sequences to enhance their capability to mimic the native environment from a biochemical point of view; (iv) the validation of the designed bioengineered tissue models from a structural, mechanical and functional point of view; (v) the design and characterization of polymeric micro/nano particles encapsulating drugs for targeted and sustained release of their payload in the developed in vitro models for testing new therapeutic approaches with the potential to answer unmet clinical challenges.

Skills and competencies for the development of the activity	We are looking for talented and motivated candidates, preferably with a Master Degree in Biomedical Engineering and with previous experience in the fields of biomaterials, nanotechnology, nanomedicine and tissue engineering. In detail, the optimal candidate should have the following skills: - Previous experience in polymer synthesis and physico-chemical characterization; - previous direct experience on in vitro cell cultures and in vitro cell experiments with biomaterials; - knowledge of methods for nanoparticle preparation and the techniques for their physico-chemical characterization; - knowledge of polymer hydrogels and the techniques for their

	physico-chemical characterization; - knowledge of surface functionalization approaches and the techniques for the physico-chemical characterization of surface functionalized constructs; - knowledge of CAD software in view of scaffold fabrication via rapid prototyping technologies. The candidate should possess a good knowledge of English Language in both written and oral forms.

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(jointly activated by Università degli Studi di Torino and Politecnico di Torino)

Research Title: NOVEL TECHNIQUES FOR AIRWAY REPLACEMENT, WITH A PARTICULAR INTEREST IN THE DEVELOPMENT OF STENTED VASCULAR ALLOGRAFT SCAFFOLDS FOR AIRWAY RECONSTRUCTION AFTER TRACHEAL AND BRONCHIAL RESECTION.

Funded by	Università degli Studi di Torino – Dipartimento di Eccellenza in "Scienze Chirurgiche"

Supervisor	Professor Enrico Ruffini enrico.ruffini@unito.it

Contact	Includere website del gruppo di ricerca, in modo che il potenziale candidato possa accedere ad altre info

Context of the research activity	After more than 50 years of research, airway reconstruction after extended resection remains a major challenge in the fields of thoracic surgery and regenerative medicine. Efforts to do this with the use of foreign materials led to chronic infection, airway obstruction, migration of the prosthesis, erosion into major blood vessels and proliferation of granulation tissue. Tracheal or bronchial allotransplantation led to unsatisfactory results due to the high rate of complications of graft necrosis or stenosis. Substantially, to date, an efficient and valid airway replacement still not exist. Indeed, even if a number of procedures of airway transplantation have been explored, all failed to demonstrate a satisfactory long-term result Promising results seem to emerge from the use of scaffolds which

	would be use as rigid structure to provide patency and rigidity of the airway, thus resembling the natural airway. Possible clinical indications include wide resection of the trachea when end-to-end anastomosis is not feasible after removal of airway tumors or long airway stenosis. The aim of the present project is to explore this new interesting area of novel techniques of airway replacement, with a particular interest in the use of allograft scaffolds, including cryopreserved aortic grafts supported by a 3D-printed tailored stent, providing a curative airway resection in patients currently excluded from surgery and destined to best-supportive care

Objectives	The aim of the present project is to explore this new interesting area of novel techniques of airway replacement, with a particular interest in the use of allograft scaffolds, including cryopreserved aortic grafts supported by a 3D-printed tailored stent, providing a curative airway resection in patients currently excluded from surgery and destined to best-supportive care. Different succeeding steps are planned, in order to provide the best evidence to the project results. To develop an integrated procedure in order to create a tailored 3d stent for airway stabilization after tracheal or bronchial resection and replacement To demonstrate in an ex-vivo model the feasibility of allograft harvesting and cryopreservation. To establish in an ex-vivo model the practicability of the implantation of a scaffold created from cryopreserved allograft and sustained by the 3D printed stent. To transfer the concept validated in ex-vivo models to an in-vivo animal model

	To apply the stented vascular allograft scaffolds model to surgery for airway stenosis and airway tumors To determine the possibility to enlarge possible indication of airway resection to patient currently exclude from surgery in reason of the extension of airway trace to resected.

Skills and competencies for the development of the activity	Design, development and evaluation of medical devices using animal models. Experienced in thoracic surgery procedure, with particular interest on Tracheal Surgery and Lung Transplantation surgery An international experience is strongly advisable

PhD in Bioengineering and Medical-surgical sciences

cycle XXXV

(jointly activated by Università degli Studi di Torino and Politecnico di Torino)

Research Title: Designing stimuli-sensitive biomaterials for biomedical applications

Funded by	Politecnico di Torino

Supervisor	Prof. Gianluca Ciardelli gianluca.ciardelli@polito.it

Contact	http://www.dimeas.polito.it/la_ricerca/gruppi/materiali_per_le_bionanotecnologie_e_laboratorio_biomedico

Context of the research activity	A great number of different biomaterials (natural and synthetic polymers, ceramics, composites and metals) has been proposed and processed during the last decades for application in the biomedical field. In particular, biodegradable polymers have been widely investigated as biomaterials for the fabrication of medical devices (e.g., catheters, vascular prosthesis), microfluidic devices, soft robots, drug-releasing systems (micro- and nano-particles) and tissue engineering /regenerative medicine scaffolds due to their easy processability and biocompatibility. Researchers have optimized several protocols to process polymers into complex architectures via conventional techniques (e.g,, freeze-drying, phase separation, gas foaming and electrospinning) or advanced technologies (e.g., selective laser sintering -SLS-, fused filament fabrication -FFF-, pressure assisted microsyringe -PAM-, stereolithography -SLA- and Bio-printing). Both natural and synthetic polymers have been investigated in the literature for biomedical application. The former have been extensively explored for clinical application due to their high biocompatibility and the advantage of inducing a weak inflammatory response. However, they usually need to be cross-linked or blended with synthetic materials to improve their mechanical properties and modulate their degradation kinetics, and they suffer for high composition variability. On the other hand, synthetic polymers play a fundamental role in the biomedical field as their properties make it

	possible to overcome some drawbacks of natural polymers; moreover, they are biocompatible and biodegradable, and show high workability and good mechanical and physical properties that can be foreseen and controlled in a reproducible manner. In this scenario, “LEGO”-like synthetic polymers, which result from the copolymerization of properly selected building blocks, are gaining more and more attention. The key advantage of this chemistry lies in the possibility to *ad hoc* design biomaterials exhibiting multifunctional properties and the potential to respond and adapt to cues coming from the environment surrounding them (e.g., concentration of ions, temperature, pH). These properties could be of high interest in the design of stimuli-responsive devices, such as shape-memory scaffolds for minimally invasive delivery of functional bioengineered constructs, stimuli-sensitive drug carriers (hydrogels, micro- and nano-particles) for the localized and triggered release of their payload and soft machines mimicking *in vitro* at the micro-scale biological processing (e.g., actuation, sensing and physico-chemical transport). In the future, these “active” devices could realistically open a new era in the biomedical field, finding widespread application in tissue engineering/regenerative medicine as reparative constructs or *in vitro* bioengineered models, for drug/therapeutic design and screening, as well as for fundamental research. Polymers that belong to the family of polyurethanes (IUPAC abbreviation PUR, but commonly abbreviated PU) are “LEGO”-like synthetic polymers, which could be designed with an enormous diversity of chemical compositions and properties. In fact, their segmented block copolymeric character endows them with a wide range of versatility in terms of tailoring their physical properties (e.g., stimuli-responsiveness), blood and tissue compatibility, and their biodegradation character. Polyurethanes possess a complex structure that typically comprises three monomers, a diisocyanate, a macrodiol and a chain extender. Because of these three degrees of freedom, a virtually infinite number of materials can be synthesized. Biomimetic synthetic PUs can be produced to elicit specific cellular functions and direct tissue formation mediated by biomolecular recognition. This goal can be achieved by both surface and bulk modifications with bioactive molecules that can incur specific interactions with cell receptors. Smart and “active” PUs can be also designed to respond to different physical or chemical stimuli, such as temperature, pH change and ionic strength. This goal could be achieved working on the chemistry of the material building blocks or through post-synthesis functionalization procedures to expose stimuli-sensitive moieties. The high potential of PUs in the biomedical field also lies in their high workability, that makes it possible to fabricate PU-based constructs via both conventional (e.g. salt leaching, gas foaming, electrospinning, phase separation) and advanced (e.g. bioprinting, fused deposition

	modelling, pressure assisted micro-syringe) fabrication technologies. This Ph.D. program is thus focused on the design and optimization of new polymeric biomaterials to be used as forming materials in the development of 3D scaffolds, micro/nano-carriers and soft actuators to be applied in tissue engineering/regenerative medicine, nanomedicine, advanced therapies and microfluidics. To this aim a new platform of stimuli-sensitive polyurethanes will be set up, thanks to the possibility to synthesize *ad-hoc* designed biomaterials suitable to a variety of fabrication technologies and applications and showing high responsiveness to physico-chemical cues. The developed strategies are expected to significantly advance the biomedical field, contributing to the definition of a new material/technology platform, which, in principle, could answer to every specific need of researchers, patients, surgeons and medical doctors.

Objectives	The Ph.D. student will be responsible for: (i) the design and characterization of new stimuli-responsive polymeric materials (polyurethanes) (ii) the processing of the newly developed biomaterials into 3D constructs and actuators via additive manufacturing techniques and micro/nano- particles for localized and prolonged drug release (iv) the introduction along polymer backbone of stimuli-sensitive moieties aiming at providing the resulting devices with the capability to respond to applied physico-chemical cues, such as temperature, ionic strength and pH. More in detail, the Ph.D. student will develop and characterize new 3D constructs, soft actuators micro/nano- particles based on *ad-hoc* synthesized stimuli-sensitive polyurethanes. This final goal will be achieved through a bottom-up approach encompassing the following steps: (i) the design and characterization of new polymeric materials belonging to the family of polyurethanes, with the aim to create a library of polymers showing a wide range of physico-chemical properties (e.g. mechanical properties, degradation kinetics, workability), processability in the form of particles, hydrogels and 3D constructs, and the potential to actively respond to external physico-chemical cues, such as temperature, pH and ionic strength changes; (ii) the microfabrication of the optimized polymeric biomaterials via advanced fabrication technologies (e.g. melt-electrospinning, bioprinting, fused deposition modeling) into 3D scaffolds and actuators for tissue engineering/regenerative medicine and microfluidics applications;

	(iii) the surface functionalization of the designed constructs with decoration moieties (e.g., proteins or peptide sequences, functional groups) to make them biomimetic and able to respond to chemical cues; (iv) the validation of the designed constructs/devices from a structural, mechanical and functional point of view; (v) the design and characterization of polymeric micro/nano particles encapsulating drugs for the targeted, sustained and triggered release of their payload in response to a physico-chemical stimulation (e.g., pH change, ionic strength, ultrasound application, temperature).

Skills and competencies for the development of the activity	We are looking for talented and motivated candidates, preferably with a Master Degree in Biomedical Engineering or related disciplines and with previous experience in the fields of biomaterial design and synthesis, nanotechnology, nanomedicine and tissue engineering. In detail, the optimal candidate should have the following skills: - Previous experience in polymer synthesis (polyurethane) and physico-chemical characterization; - Previous experience in biomaterial processing and characterization; -Knowledge of methods for nanoparticle preparation and the techniques for their physico-chemical characterization; - Knowledge of polymer hydrogels and the techniques for their physico-chemical characterization; - Knowledge of surface functionalization approaches and the techniques for the physico-chemical characterization of surface functionalized constructs; - Knowledge of CAD software in view of scaffold fabrication via rapid prototyping technologies. The candidate should possess a good knowledge of English Language in both written and oral forms.

PhD in Bioengineering and Medical-Surgical Sciences

cycle XXXV

(jointly activated by Università degli Studi di Torino and Politecnico di Torino)

Research Title: Molecular Basis of Subcellular Mechanics

Funded by	Politecnico di Torino

Supervisor	Prof. Marco Agostino Deriu, Prof. Umberto Morbiducci

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Context of the research activity	The integration of multiscale, multiphysics models results topical in the study of a hierarchically organized, complex system such as a subcellular structure or even a cell. This hierarchical modelling has the capability of elucidating relationships subsequent tissue growth/remodelling/adaptation. This emerging scientific paradigm strongly depends on state-of-the-art instruments allowing for integration through various scales in a multidisciplinary vision. The recent progress in generating computational modelling tools allows for an effective implementation of hierarchical scales ranging from the atomic level, to the mesoscale focus of coarse-grained procedures, reaching the continuum macroscale. Therefore, the result of this integration should be a multiscale/multiphysics modelling framework able to move not only through-scales, but also from chemistry to mechanics. This approach promises to revolutionize the way we understand the cell and its emergent properties depending by a complex interaction among cell constituents. The employed approach encompasses the need, within the scientific community, for hierarchical simulation models investigating different levels of resolution and incorporating these levels in a multi-scale approach to analyze molecular and subcellular reasons driving cell mechanics.

Objectives	The main objectives will be focused on the implementation of molecular and multiscale techniques that takes into account the

	hierarchical and complex organization characterizing cell cytoskeleton and/or subcellular structures. This computational modelling framework will be designed to investigate the relationship between atomistic level phenomena and subcellular mechanical behavior of the cytoskeleton filaments and networks, which depends on dynamics of polymerization/depolymerization of cytoskeleton filaments and their interconnection through cytoskeleton binding proteins and/or ligands. For example the molecular dynamics concerning the interaction between specific binders (other proteins, compounds, or nanoparticles) will be studied to shed light on folding phenomena which may be related to the ability of the building block to assembly in the filament. Coarse grained modelling and continuum approaches fed by data from molecular level simulations and experiments will allow to unravel how phenomena at the nanoscale affect filament properties including their dynamics of self-aggregation/ organization.

Skills and competencies for the development of the activity	We are looking for talented and motivated candidates with a Master Degree in Biomedical Engineering and with previous experience in the fields of molecular modelling with focus on atomistic and coarse grained molecular dynamics, enhanced sampling, dimensionality reduction techniques, data clustering, docking calculations, characterization of ligand affinity, intra- and extra-cellular kinetics. The candidate should also have high confidence with Linux environment and ability to deal with HPC clusters, such as CINECA. The candidate should possess a good knowledge of English Language in both written and oral forms.

PhD in Bioengineering and Medical-Surgical Sciences

cycle XXXV

(jointly activated by Università degli Studi di Torino and Politecnico di Torino)

Research Title: Experimental Characterization of Biological Tissues: From The Micro to the Macro Passive and Active Physical Properties

Funded by	Politecnico di Torino

Supervisor	Prof. Alberto Audenino *(email: alberto.audenino@polito.it)* Prof. Cristina Bignardi *(email: cristina.bignardi@polito.it)*

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Context of the research activity	Bioengineering is a multidisciplinary research field that brings together engineering, medicine, biology, physics, chemistry, mathematics, with the key aims to advance knowledge and to support the development of ground-breaking diagnostic and therapeutic strategies. In biological tissues, topography, microarchitecture, and passive and active mechanical properties are features fundamental in regulating cell behaviour and homeostasis, promoting tissue regeneration, and directing development of tissues and pathologies. Therefore, understanding and quantitatively measuring such micro and macro-scale properties become essential for a deep understanding of physiological and pathological processes based on mechanobiology, for the development of in-vitro models, and for finally designing advanced therapeutic strategies. Accurately characterising passive and active physical properties of biological tissues is highly challenging due to the intrinsic complex nature of biological tissues. Indeed, the macroscopic behaviour of a tissue is governed by its intrinsic material properties, but also by its overall geometry and the boundary conditions acting upon it. Therefore, a multiscale and multidisciplinary approach will be

	adopted and a synergic interaction between bioengineering and biotechnological knowledge will be crucial. The PhD student will rely on the competences and the facilities of the PoliToBIOMed Center, an interdepartmental structure born with the ultimate goal of enabling technologies for personalized medicine. As concerns experimental activities, the PoliToBIOMed Center is equipped with several testing and analysis machines (uniaxial/biaxial static/dynamics, hard tissue nanoindenter, soft tissue nanoindenter, TEM, spinning disk, etc.). For computational tasks, PoliToBIOMed Center is equipped with SUN cluster composed by 1 rack quad core Workstation SunFire X4450 and 6 Quad-core rack workstations SunFire X4450 (106 CPUs).

Objectives	The research objectives of the PhD program will be: 1) Multiscale characterization of biological tissues and cells, based on different set-ups at the macro (i.e., uniaxial/biaxial tensile testing, permeability testing,) and micro-scale (i.e., morphology TEM analisys, nanoindentation, micropillars), in order to capture the typical passive and active features of biological tissues and cells under investigation 2) Development of constitutive models for biological tissues, in terms of mechanical behaviour and biotransport phenomena, for describing the relations among physical quantities. In combination with experimental data, the parameter fitting will be performed by using nonlinear optimization schemes, considering irregularities and inhomogeneities of the investigated tissues The final aim of the research will be to provide guidelines for several issues related to the multiscale characterization of biological tissues and to define standardized testing methods and protocols.

Skills and competencies for the development of the activity	We are looking for talented and motivated candidates, preferably with skills/experience in: Biological tissue experimental characterization, Image and data processing, Computer programming, Technical drawing, Teamwork, Aptitude to work with multidisciplinary teams, written and spoken English Language.

PhD in Bioengineering and Medical-Surgical Sciences

cycle XXXV

(jointly activated by Università degli Studi di Torino and Politecnico di Torino)

Research Title: Home Care and Telemedicine

Funded by	Politecnico di Torino -DET (Azioni di incentivazione del dottorato)

Supervisor	Gabriella Balestra (gabriella.balestra@polito.it), Marco Knaflitz (marco.knaflitz@polito.it), Filippo Molinari (filippo.molinari@polito.it)

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Context of the research activity	Due to the ageing of the population, the need for home care assistance is increasing every year, in terms of number of patients as well as of the complexity associated to comorbidities. These conditions led in recent years to an increased interest of healthcare facilities on telemedicine applications. In our territory, a master program in Telemedicine was recently started by Politecnico di Torino in cooperation with ASL TO4. Telemedicine refers to systems used in clinical practice that are taking advantage of communications technology. Several other technical components contribute to the goodness of these systems: sensors, portable and wearable devices, signals and image processing algorithms, data integration methods, and service design by means of modeling and simulation tools. Several pilot projects in telemedicine, usually based on telemonitoring platforms, have been reported in literature with promising results, but only a few applications became routine

	assistance services. Several problems are associated with this difficulty. From a management point of view most of the projects do not provide solutions that can be directly applied to routine daily assistance, but their goal is only to demonstrate the feasibility of using a specific device. Because they rely on highly motivated patients that are using the devices for a limited period of time, the daily usability problems are often underestimated. Another limitation is that these projects only address a specific pathology while ignoring possible comorbidities, which require the integration of all patient data to support the clinical staff in detecting potential critical changes in the clinical status. Hence, by summarizing, these approaches lacks the capability of generalizing and merging together multivariate clinical data. Moreover, from a technical point of view, there is still the necessity to develop new wearable devices to increase the data available for patient monitoring. Another of the limits of studies reported in literature is that they are not taking into account the fact that often different physicians are in charge of the same patient. Several experts believe that care coordination and patient management could be planned more effectively and efficiently through telemedicine. Last but not least there are still few studies in literature that effectively present applications that are patient centered and/or that can lead the patients and the caregivers to contribute to the assistance (patient empowerment). Thus, to make technology and services more suitable for the elderly as well as for patients affected by severe chronical diseases with comorbidities, there is still the necessity to carry out research in: a) Developing new assistance models based on telemedicine technologies b) Developing new portable/wearable devices for the acquisition and processing of physiological parameters c) Developing intelligent systems able to cope with the large amount of data collected for each patient to point out important information and to alert physicians and nurses when there are critical changes in the patient clinical status.

Objectives	The PhD project will begin by outlining the requirements of a general home care service and will continue by developing the new technologies and devices necessary to support the daily assistance activities. The developed technologies and devices will be complementary to what is available on the market. The specific objectives to reach during the three years of the doctoral program will be: a) Modeling and analysis of existing home care services by

	means of process modeling techniques to understand how telemedicine can improve quality of care and patient empowerment b) Development of wearable devices to be included in monitoring platforms c) Development of systems based on machine learning to support the intelligent management of a large collections of data d) Development of new assistance models and of simulation packages to assess the feasibility of the implementation of the assistance service in terms of human and technological resources e) Validation of the developed technologies in the real context.

Skills and competencies for the development of the activity	The candidate must have the *Laurea Magistrale* degree in Biomedical Engineering. He/she must be well trained on - biomedical instrumentation - biomedical signal processing - machine learning applied to analysis and interpretation of biomedical data, medical images and biomedical signals Competencies on the modelling of clinical processes are welcomed.

PhD in Bioengineering and Medical-Surgical Sciences

Cycle XXXV

(jointly activated by Università degli Studi di Torino and Politecnico di Torino)

Research title: BIOROBOTICS: MINIMALLY INVASIVE SURGERY IN ORTHOPAEDIC TRAUMA AND ROBOTS FOR REHABILITATION

Funded by	Centro Polito^{BIO}Med Lab - Centro PIC4SeR - DIMEAS – Politecnico di Torino (Azioni di incentivazione del dottorato)

Supervisor	Prof. Alberto Audenino *(email: alberto.audenino@polito.it)* Prof. Marcello Chiaberge (*email: marcello.chiaberge@polito.it*) Prof. Stefano Pastorelli *(email: stefano.pastorelli@polito.it)*

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Context of the research activity	The National Research Program (PNR) 2015-2020 indicates 12 strategic fields of research, one of which is called “Health”, in line with one of the mail tracks of the H2020 program. In the Health track, the PNR strategically promotes also researches devoted to the improvement of nutrition and quality of life. In this national and international scenario, the activities of the Polito^{BIO}Med Lab play a central role in providing: i) new technologies for health and life science; ii) expected economic and sustainable impact on health systems; iii) development of new approaches for a personalized medicine; iv) focus on elderly, fragile subjects, and societal challenges; v) research focused on widespread pathologies; vi) expected technological transfer and vii) increase in fund-raising opportunities. From this perspective, a key role in the field of advancing technologies for health is played by biorobotics. Nowadays robotic technologies are increasingly spreading in several scenarios: from the daily living to clinical areas. Biorobotics is more and more entering the medical practice, assisting clinicians and surgeons in trauma and orthopedics, minimally invasive surgery, laparoscopic devices as well as rehabilitation orthoses. From this perspective, the research of novel in-silico solutions, coupled to a better understanding of physiological systems through experimental investigations, could lead to the development of new and more effective systems and devices. Computer Assisted

	Orthopaedic Surgery (CAOS), although cited since 1990, is still an active research discipline bringing together orthopedic surgeons with traditionally technical disciplines, such as engineering, computer science and robotics. The key idea behind CAOS is that operative outcomes will be strongly improved through the use of computer technology. CAOS technologies can indeed allow to plan operations an advance, to get feedbacks in real time in the operation room, as well as to measure and evaluate post-operative outcomes. The PhD student will rely on the competences and the facilities of the Polito^{BIO}Med Lab and of the PIC4SeR Interdepartmental Center. As concerns experimental activities, the Polito^{BIO}Med Lab is equipped with several testing and analysis machines (uniaxial/biaxial static/dynamics mechanical testing systems at the macro- and micro-scale, gait analysis system, vital signals acquisition systems, etc.) and manufacturing devices (3D printers, Computer Numerical Control (CNC) Machines). For computational tasks, Polito^{BIO}Med Lab is equipped with SUN cluster composed by 1 rack quad core Workstation SunFire X4450 and 6 Quad-core rack workstations SunFire X4450 (106 CPUs).

Objectives	The research objectives of the PhD program for the transfer of technologies from engineers to clinicians will be: 1) Design of software and hardware systems aimed at the improvement of computer aided and minimally invasive surgery, to increase surgeon precision or reduce operator-dependent risk of errors. 2) Development of subject-specific computational models able to integrate Computer Assisted Orthopaedic Surgery (CAOS) systems. 3) Development of rehabilitation orthoses equipped with sensors aimed at kinematics analysis and with actuators to assist rehabilitation and movement The aim of the Doctoral program involves the design of systems allowing the extraction of quantitative measures necessary to advance the current gold standards in clinics and surgery and the design of software and hardware system within Computer Aided and minimally invasive surgery.

Skills and competencies for the development of the activity	We are looking for talented and motivated candidates, preferably with skills/experience in: experimental data acquisition, 3D prototyping, multibody and Finite Element (FE) modelling, Image and data processing, Mechatronics and Control, Computer programming, Technical drawing, Teamwork, Aptitude to work with multidisciplinary teams, written and spoken English Language.

PhD in Bioengineering and Medical-Surgical Sciences

Cycle XXXV

(jointly activated by Università degli Studi di Torino and Politecnico di Torino)

Research Title: Microfluidic light induced 3D bioprinting: lifelike organ-on-a-chip models for drug screening

Funded by	Centro Interdipartimentale Polito^{BIO}MedLab - Politecnico di Torino (Azioni di incentivazione del dottorato)

Supervisor	Candido Fabrizio Pirri (fabrizio.pirri@polito.it) Francesca Frascella (francesca.frascella@polito.it) Mara Terzini (mara.terzini@polito.it) Kristen Mariko Meiburger (kristen.meiburger@polito.it)
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Context of the research activity	Bioengineering is a multidisciplinary research field that brings together engineering, medicine, biology, physics, chemistry, mathematics. Bioengineering aims to advance knowledge and create tangible applications in medicine and biology. In this context, the Interdepartmental Center Polito^{BIO}MedLab aims at establishing a unique concept of excellent research taking advantage of a 'multidisciplinary genetic code'. In particular, nanostructured materials and nanotechnologies for biotech and biomedical applications have produced several success stories at Politecnico di Torino, as a consequence of the establishment and growth of several research groups in the field. The subjects covered have a strong international importance. In this framework, bioprinting is a revolutionary technology to assemble scaffolds for growing tissues. Microfluidic organs-on-a-chip is a useful platform with widespread applications mainly in drug screening and pathological studies. Organ-on-a-chip models are created to recapitulate the structural, microenvironmental and physiological functions of human organs. Recently, bioprinting has been applied to fabricate organ-on-a-chip models owing to its ability to print multiple materials and cell types simultaneously with good spatial resolution and reproducibility. This enables the creation of a biomimetic microenvironment with heterogeneous 3D

	structures. Functional vascularized tissue structure can be printed directly enabling fluid flow for transport of nutrition, gaseous exchange and removal of waste.

Objectives	Traditional in vitro culture models are unable to fully reflect the organ microenvironment owing to the difference in terms of cell morphology, protein expression, cell–cell and cell–matrix interactions, and drug response. By contrast, the flexibility of bioprinting modes allows deposition of biomaterial–cell spheroid–tissue in any free-form-inspired complicated 3D structures on the chip, creating cell culture models tailored for studying cell–cell and cell–matrix interactions. During the research project, the following tasks will be pursued: - Study and optimization of 3D bio printable formulations with the choice of monomers that can assure the desired final properties - Study of the biomechanical properties of the printable formulation, through nanoindentation test - Study the usefulness of this bioprinted construct for drugs testing in a contest of personalized medicine. - Use of the *in vitro* culture bioprinted as a model for physiological microvascular phantom The candidate will work in the framework of the Polito^{BIO}MedLab, in order to enhance the interconnection between the multidisciplinary research field of the Center. The candidate will operate mainly on the instrumentation settled in the Polito^{BIO}MedLab, in particular with the 3D bioplotter, the spinning disk confocal microscope, the photoreometer and all the mechanical characterization technique, in addition to the biological ones.

Skills and competencies for the development of the activity	We are looking for talented and motivated candidates, preferably with a Master Degree in Biotechnology and with previous experience in the fields of cellular and molecular biology. In detail, the optimal candidate should have previous direct experience on in vitro cell cultures and in vitro cell experiments with biomaterials.