SUBMISSION FORM OF PROPOSALS FOR DOCTORAL RESEARCH PROJECTS

Objective of the Doctoral Programme in Health Sciences and Technologies

The objective of the new interdepartmental Doctoral Programme in Health Sciences and Technologies is to train the next generation of leaders in industrial, clinical, and academic research. Our goal is to develop an organic research programme at the interface between engineering and medicine, which is inspired by the quantitative and integrative approach of physical sciences, and by the latest development in biomedical research, drive the development and clinical translation of disruptive health technologies.
The doctoral training programme will prepare students in conducting research which:
- Extend the comprehension of how human physiology and pathology work in term of physical and chemical mechanisms, and how these mechanisms respond when perturbed by external factors such as therapies, changes in life style, and environmental factors;
- Develop new technologies that by leveraging on this mechanistic understanding pursue a wide spectrum of applications relevant to human health, including prevention, diagnosis, prognosis, treatment, and rehabilitation.

Procedural aspects on the submission of proposals for doctoral research projects

Every year the PhD process will start with the submission of proposals for doctoral research projects. Each proposal must be submitted jointly by two supervisors, one providing the clinical expertise, the other the technological expertise. The Project Selection Committee will select a number of projects that is three times the number of available scholarships and should be distributed in similar proportion between medical-led or technology-led proposals. The resulting list of projects will be included in the call for student applications that the Executive Committee will compile soon after. Each student, depending on their degree, will be able to apply only for a sub-set of projects; among them each student will be allowed to select three projects, and name them in order of preference; however, in some cases it might not be possible to satisfy all requests, and some students might be offered a research project different from those they selected.

Doctoral training program

In order to be admitted to the selection, a student needs a five-year higher education degree, which includes at least one module for each of the following disciplines: mathematics, physics, computer science, biology, physiology, and anatomy.

Max number of proposals for each member of the Academic Board: 3 (three)
Max number of selected projects for each member of the Academic Board: 2 (two)
Max number of selected projects for 2019: 12 (twelve)

Title of the project

Innovative Methods for Objective Pain Measurement

Student's degree (you can choose more than one, if needed)

Yes/Not	Cultural area
Not	Medicine, biology, or related disciplines
Yes	Engineering, physics, mathematics, computer science, chemistry, materials science or related disciplines

Student's skills (you can fill more than one field, if needed)

Cultural area	Skills
Medicine, biology, or related disciplines	Neurophysiology
Engineering, physics,	Biomedical Engineering with special skills on biomedical signal processing, wearable sensors and mobile health

mathematics, computer science, chemistry, materials science or related disciplines	

Tutors (2, from different cultural areas and with at least 1 from the Academic Board)

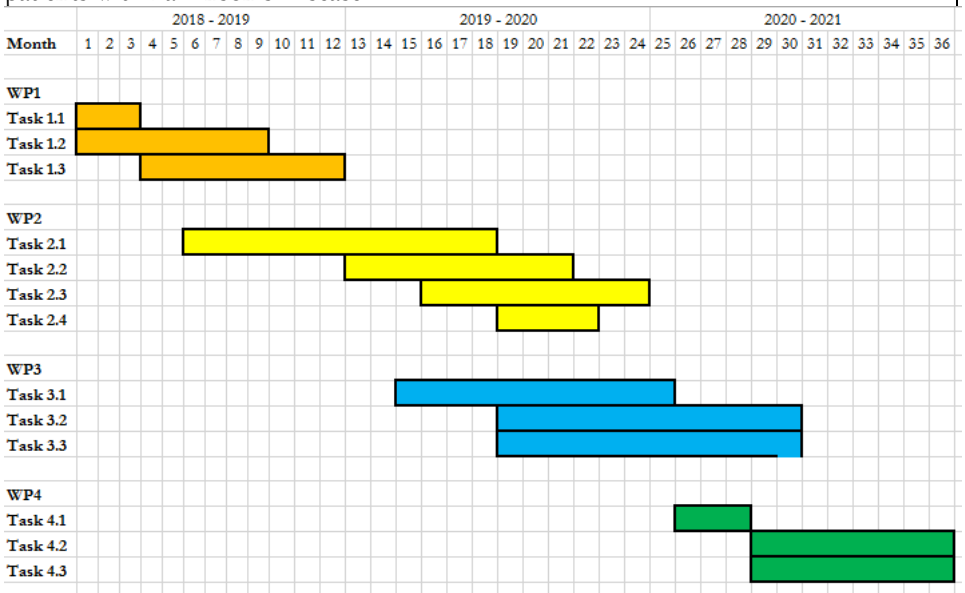
Cultural area	Name & Surname	Department
Medicine, biology, or related disciplines	Prof. Stefano Canestrari Dott. Igor Diemberger	Dipartimento di Scienze Giuridiche (DSG) Dipartimento di Medicina Specialistica, Diagnostica e Sperimentale (DIMES)
Engineering, physics, mathematics, computer science, chemistry, materials science or related disciplines	Prof. Lorenzo Chiari	Dipartimento di Ingegneria dell'Energia Elettrica e dell'Informazione "Guglielmo Marconi" (DEI)

Research project

	Synthetic description
Summary (max 1000 chars)	Pain is an unpleasant subjective experience. At present, clinicians are using self-report or pain scales to recognize and monitor pain. Objective assessment of pain is a topic of great interest, although relatively unexplored, both in clinical and scientific research. The present PhD project will investigate, design and experimentally validate innovative methods for the evaluation of pain and psychophysical state through measurement of neurophysiological signals recorded by personal health systems. This project stems from previous methodological research activities carried out at the Personal Health Systems Lab at DEI in the field of wearable devices, and will build its innovation potential on the side by side cooperation with a variety of clinical experts (e.g. cardiologists, neurologists, oncologists, and psychologists), who shall provide their expertise to advance the knowledge and identify solutions for the measurement and relief of specific pain conditions.
Objectives (max 1000 chars + max 5 relevant references)	The main objective of this project is to improve our ability to quantify pain with the aid of non-invasive techniques. This will go through: • Definition of data and signal processing techniques aimed at identifying pain-sensitive parameters • Development of non-invasive tools for the evaluation of pain and psychophysical state through measurement of psychophysiological signals • Definition of standardized protocols, based on wearable sensors, to be used in clinical settings This will allow a significant step towards more reliable pain assessments and a targeted innovation for palliative medicine. In terms of training, this project will create a biomedical engineer with strong expertise in the area of advanced signal processing and wearable device integration and optimization, and with a unique capability of collecting and interpreting inputs from clinicians, with full awareness of the bioethical dimension of his/her research.
Rationale and scientific background y (max 2000 chars+ max 5	The tools available today to evaluate painful sensations are self-assessments, scales, and interviews. These techniques are widely influenced by the subjective perception of the individual. The reduced cognitive skills and the poor collaboration between the evaluator and the individual further limit the reliability of the measure. Scientific research is recently producing important contributions on the neurophysiological mechanisms underlying pain. It is known that the autonomic nervous

relevant references)	system (ANS) plays a fundamental role in painful sensations, causing variations in the performance of various psychophysiological variables, such as heartbeat, blood pressure, electrodermal activity, temperature, and movement. These parameters might serve as indicators and could allow an objective measure of the patient's pain status, bringing benefits in several aspects: i) evaluation of the effectiveness of therapies or new experimental approaches, ii) correct management of antalgic therapy, iii) more in-depth knowledge of neurophysiological mechanisms involved in pain. The biological signals involved in painful sensations can be acquired via non-invasive wearable sensors. Continuous monitoring, carried out during the daily routine, is desirable for more in-depth characterization of the psychophysical health state. The knowledge of these dynamics is also relevant in a multitude of clinical applications. The growing demand for objective and non-invasive measures of the health and wellbeing of a subject, as reflected by autonomic signals, indeed embraces several domains, including neurology (e.g. detecting freezing of gait or non-motor symptoms of Parkinson's Disease) and cardiology (e.g. heart rate variability as a potential marker for resilience and behavioral flexibility). There is a strong demand in the clinical field of objective measurement techniques that can establish the real psychophysical state of the patient. To date, the lack of standardization in the methods of identification and analysis of neurophysiological variables represents a strong limitation on progress in this sector. ***References*** ▫ Subramaniam S., Doss B., Chanderasekar L. *et al.*, "Scope of physiological and behavioural pain assessment techniques in children – A review", *Healthcare Technology Letters*, (5), 4, 124-129, 2018 ▫ Lopez-Martinez D., Picard R., "Multi-task Neural Networks for Personalized Pain Recognition from Physiological Signals", *Seventh International Conference on Affective Computing and Intelligent Interaction Workshops and Demos (ACIIW)*, San Antonio, TX, 2017 ▫ Roue J., Rioualen S., Gendras J. *et al.*, "Multi-modal pain assessment: are near-infrared spectroscopy, skin conductance, salivary cortisol, physiological parameters, and Neonatal Facial Coding System interrelated during venipuncture healthy, term neonates?", *Journal of Pain Research*, (11), 2257-2267, 2018 ▫ Castaneda D., Esparza A., Ghamari M. *et al.*, "A review on wearable photoplethysmography sensors and their potential future applications in health care", *International Journal of Biosensors & Bioelectronics*, (4), 4, 195-202, 2018
Preliminary results if existing (max 1000 chars+ max 5 relevant references)	Several experimental studies in the literature confirm the sensitivity of physiological signals to nociceptive stimulation. The majority of these studies are focused on the analysis of the differences between presence and absence of pain. It has been demonstrated experimentally how the behavior of different physiological variables (e.g. heart rate and measures taken from the analysis of heart rate variability, skin conductance, surface temperature) is influenced by the perceived pain. The Personal Health System Lab is a partner of the Look of Life project promoted by ANT. The project is testing the use of innovative technologies, such as immersive reality, for palliative care at home, in order to reduce the negative impact that isolation can have on cancer patients and mitigate their pain. The team has developed solutions for biomedical signal processing, motor performance assessment, fall risk assessment, and virtual rehabilitation. It regularly designs and makes use of wearable sensors, advanced statistical models, and artificial intelligence solutions. ***References*** ▫ Cavalcanti S., Severi S., Chiari L., et al., "Autonomic nervous function during haemodialysis assessed by spectral analysis of heart-rate variability", *Clin Sci (Lond)*. 1997 Apr;92(4):351-9 ▫ Di Marco L.Y., Chiari L., "A wavelet-based ECG delineation algorithm for 32-bit integer online processing", *Biomed Eng Online*. 2011 Apr 3;10:23.

	▫ Lopane G., Mellone S., Chiari L., et al., "Dyskinesia detection and monitoring by a single sensor in patients with Parkinson's disease", *Mov Disord.* 2015 Aug;30(9):1267-7. ▫ Palmerini L., Rocchi L., Mazilu S., Gazit E., Hausdorff J.M., Chiari L., "Identification of Characteristic Motor Patterns Preceding Freezing of Gait in Parkinson's Disease Using Wearable Sensors", *Front Neurol.* 2017 Aug 14;8:394 ▫ Mincolelli G., Marchi M., Chiari L. *et al.*, "Inclusive design of wearable smart objects for older users: design principles for combining technical consraints and human factors", *AFE International Conference on Design for Inclusion*, (776), 324 – 334, 2019
Research project including methodology (max 5000 chars)	The doctoral project is based on an interdisciplinary approach to the problem, essential in the field of instrumental measurements on neurophysiological signals. The candidate will spend about 65% of the time in the Personal Health Systems Lab, where he will be able to deepen his/her skills on wearable sensors and analysis of biomedical data and signals. For 25% of the time, the candidate will work in the clinical settlement to run small pilots, identify the critical issues that may occur in the instrumental measurements of psychophysiological variables, and explore possible applications of the methods developed in different contexts. Finally, the candidate will spend about 10% of the time to investigate the legal and bioethical implications of introducing technologies in the field of pain assessment. The student will apply his/her interdisciplinary skills gained in the early stages of the research project in experimental studies thanks to collaborations in place with social and clinical partners, such as the ANT foundation (National Cancer Association), the U.O. Cardiologia at the S.Orsola-Malpighi Hospital, and the ISNB-Bellaria Hospital. The PhD student will also have the opportunity to undertake a period of training in one of the international research centers collaborating with the Personal Health Systems Lab, e.g., for this project, the University College Dublin or the MIT Media Lab. The research project will be organized into four work packages. **WP1: Study and analysis of the pathophysiology of pain** **Task 1.1** Systematic review of the literature on neurophysiology of pain. The student will deepen and consolidate his/her knowledge in the field of neurophysiological signals, with particular attention to autonomic signals (i.e. sensitive to the activation of the autonomic nervous system). **Task 1.2** Overview of available HW / SW platforms. The student must constantly update on the development of innovative wearable sensors suitable for monitoring physiological parameters of physiological signals sensitive to the activation of the autonomic nervous system (e.g. photoplethysmographic signal, electrodermal activity, skin temperature, movement). **Task 1.3** Analysis and selection of reliable methods among those proposed in the literature for the evaluation of sensor-based neurophysiological parameters. The student will apply his/her knowledge so far developed to the critical selection of evaluation techniques aimed at measuring the neurophysiological response through wearable sensor signals. **WP2**: **Set-up and testing of solutions for the evaluation of various physiological subsystems through personal health systems** **Task 2.1** Development of algorithmic prototypes for the analysis of autonomic nociceptive and nervous system **Task 2.2** Exploratory study of psychophysiological parameters on healthy subjects. The student will apply the in-depth methodologies selected in WP1 for the evaluation of physiological changes/fluctuations of the selected variables **Task 2.3** Statistical analysis on the results obtained in Task 2.2. The candidate will use statistical techniques for the evaluation of physiological parameters obtained from healthy subjects, elaborating models suitable for the description of physiological changes **Task 2.4** Legal and bioethical implications of introducing technologies in the field of pain assessment **WP3**: **Experiments on pathological subjects suffering from chronic and acute pain**

	Task 3.1 Experimental tests on oncological patients within the "Look of Life 2.0" project, in collaboration with ANT. The student will work in close contact with the Foundation's psychologists and neurologists, in order to identify effective strategies for pain assessment **Task 3.2** Statistical analysis on the results obtained in Task 3.1. Outcomes of the experimental study will be evaluated. **Task 3.3** Comparison of the results obtained on healthy and pathological subjects. The comparison will be based on the results produced in WP2 and WP3. **WP4**: **Translation of developed methods in selected case studies (e.g. neurological and cardiovascular)** **Task 4.1** Insights on the possible transferability of the techniques and methodologies developed in previous WPs to selected case studies from the neurological and cardiovascular fields. The candidate will explore the possibility of extending the applicative domain of the methodologies learned and consolidated in WP2 and WP3. **Task 4.2** Case study 1: Mobile monitoring of physiological parameters representative of cardiovascular health. **Task 4.3** Case study 2: Mobile monitoring and evaluation of non-motor symptoms in patients with Parkinson's Disease 
Innovation potential (scientific and/or technological) (max 1000 chars)	From a technical and scientific point of view, this project will translate to a better understanding of the physiological mechanisms underlying pain. More specifically:: • Definition of methods for the objective evaluation of pain, currently of great interest in scientific research and for which there is no standard • Estimation of parameters sensitive to physiological changes caused by the activation of the autonomic nervous system • Possible definition of normative values for homogeneous subgroups, thanks to the comparison between different cohorts • Introduction in the clinical field of new methods for monitoring patients, both in hospital and in outpatient settings
Expected results and applications to human pathology and therapy (max 1000 chars)	From a translational point of view, the knowledge developed could have, on the long term, a strong impact on the clinical management of the patient. The objective assessment of pain would indeed result in a more reliable assessment of the effectiveness of a therapeutic intervention and in a more precise administration of the antalgic therapy. Such tools would therefore provide an improvement in terms of patient quality of life, in addition to scientific progress in this field. A better knowledge and management of autonomic signals could favor mobile health solutions and hence de-hospitalization, remote monitoring and, hopefully, the early identification of symptoms and the early diagnosis of both neurological and cardiovascular diseases.

Available resources for the project

	Synthetic description
Research environment (labs involved, background, and location)	Personal Health Systems Lab, Dipartimento di Ingegneria dell'Energia elettrica e dell'Informazione "Guglielmo Marconi" – DEI Fondazione ANT Unità Operativa di Cardiologia – Ospedale Sant'Orsola-Malpighi ISNB - Reparto di Neurologia – Ospedale Bellaria
Main equipment (facilities and location)	The Personal Health Systems Lab is equipped with most of the facilities required for this project, including gold-standard systems for cardiovascular measures.
Additional funding (title, amount, start date, duration)	No significant costs are expected on behalf of DSG and DIMES, most of the research and training costs will be covered within DEI. Funding already available at DEI will cover the cost for additional equipment needed for experimental validation of the proposed solutions.

International collaborations for the project (also in view of the Student's secondment)

	Project	Location and team
#1		University College Dublin, School of Psychology
#2		MIT Media Lab (Wearable computing)