PhD Program in Bioengineering and Robotics

Curriculum Bioengineering

Research themes

Bioengineering is a discipline that integrates physical, chemical, mathematical, computational sciences and engineering principles to study biology, medicine, behavior, and health.

Bioengineering advances fundamental concepts, creates knowledge from the molecular to the organ systems levels, and develops innovative biologics, materials, processes, implants, devices, and informatics approaches for the prevention, diagnosis, and treatment of disease, for patient rehabilitation, and for improving health and well-being (NIH Working Definition of Bioengineering—July 24, 1997).

The PhD curriculum in Bioengineering implements the evolution of a long-standing tradition of the Bioengineering School of the University of Genova, characterized by a marked *experimental* and *technological* vocation, providing advanced training and research experience for graduate students interested in: *in vitro* electrophysiology, cellular mechanobiology, microscopy, tissue engineering, neural control of the movements, motor learning and neuromotor recovery, as well as neuroengineering, micro- and nano-technologies, assistive and rehabilitation technologies, integrated perceptual systems.

The research activities, mainly conducted at the Department of Informatics, Bioengineering, Robotics and System Engineering (DIBRIS), cover a variety of areas and offers potential collaborations with other departments at the University of Genova, as well as with leading national and international research institutions. This will ensure a unique scientific environment to the students to carry out international research projects.

The main research interests lie within the following broad themes:

- Neuroengineering
- Molecular and cellular engineering
- Interaction and rehabilitation engineering
- Health informatics

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 different research themes. This will be obtained also by planning exchange of students for 6 to 12 months with national and international laboratories where particularly interesting experimental techniques and/or strategic scientific approaches are well established.

The ideal candidates are students with a higher level university degree willing to be involved in multidisciplinary studies and to work in a team of scientists coming from different background but sharing common objectives. The proposed themes are presented in details in the following indicating tutors and place where the research activity will be developed.

International applicants are encouraged and will receive logistic support with visa issues, relocation, etc.

1. Unobtrusive wearable sensors for advanced biomedical applications

Tutors: Danilo Pani, Annalisa Bonfiglio

Department: Dept. of Electrical and Electronic Engineering, University of Cagliari, http://dipartimenti.unica.it/ingegneriaelettricaedelettronica/

Description: Wearable sensing is a growing research field. The advancements of the research on electroconductive polymers now allow the selective functionalization of a textile substrate to create electrodes, electrochemical and mechanical sensors. The lack of adhesion of these sensors to the skin, especially when used in dry conditions, and the nature of the substrate, limit the field of applications of textile sensors. More recently, ultra-conformable sensors based on nanofilms, usually referred to as "tattoo electrodes", are entering the physiological sensing arena, opening hitherto unthinkable applications, thanks to their incomparable adhesion without electrolytes, conformability able to follow the skin wrinkles, transparence and light weight. The aim of the proposed research theme is to develop, study and characterize wearable sensors based on ultra-conformable substrates, for advanced biomedical applications where the unobtrusiveness of the monitoring, the substrate conformability, its comfort and/or its transparency are essential qualities. The impact on the personalized medicine will be also investigated. Main application areas of interest are high-density EMG, invasive and non-invasive ECG, biomechanical sensing. Specific applications will require the adoption of advanced signal processing and machine learning tools for the processing and automated analysis of the signals gathered from these sensors, e.g. for prosthetic and assistive devices.

Requirements: background on physiology, electrophysiology and bioengineering methods. Proficiency in the use of Matlab for signal processing, basic knowledge of machine learning and digital microarchitectures. Attitude for laboratory activity, including development of devices and their validation.

References:

Viola FA, Spanu A, Ricci PC, Bonfiglio A and Cosseddu P. (2018). Ultrathin, flexible and multimodal tactile sensors based on organic field-effect transistors. *Scientific Reports*.

Achilli A, Bonfiglio A and Pani D (2018) Design and Characterization of Screen-Printed Textile Electrodes for ECG Monitoring. *IEEE Sensors Journal*, vol. 18, no. 10, pp. 4097-4107.

Pani D, Usai I, Cosseddu P, Melis M, Sollai G, Crnjar R, et al. (2017) An automated system for the objective evaluation of human gustatory sensitivity using tongue biopotential recordings. *PLoS ONE* 12(8): e0177246.

Contacts: danilo.pani@unica.it; annalisa.bonfiglio@unica.it

2. Decoding the neurophysiology of locomotor control in Parkinson's disease

Tutor: Canessa Andrea

Department:

https://www.dibris.unige.it/

https://www.hci.uni-wuerzburg.de/

https://www.wurzburg-neuroscience.de/isaias

https://www.parkinson.it/centro-parkinson.html

Description: Gait disturbances are a common and severe problem of Parkinson's disease (PD) poorly responsive also to advanced treatments, like deep brain stimulation (DBS). Freezing of gait (FOG) is a peculiar gait derangement in PD and it is characterized by the inability to produce effective stepping causing falls, mobility restrictions, and poor quality of life. The pathophysiology of FOG is still unclear also because of the episodic and unpredictable nature that greatly challenges its recording and evaluation. Virtual Reality (VR) can overcome this limitation by replicating real-life situations triggering FOG in a controlled environment. The study proposed aims to investigate the supraspinal locomotor control in patients with PD and FOG through a novel and integrated multimodal approach. In particular, we will collect detailed neurophysiological recordings of corticosubcortical dynamics (with hdEEG and implanted electrodes for DBS), biomechanics measurements, including surface electromyography, and functional and molecular brain imaging data (i.e. fMRI and FDG PET). Gait analysis will be performed in several VR environments recreating the situation of real-life usually triggering gait freezing. A computational model of the pathological dynamics of the locomotor circuits will merge all these complementary results for future personalized treatments. In the context of neurorehabilitation and neuromodulation, VR technology will foster the delivery of meaningful and patient tailored therapies promoting motor functional recovery.

Requirements: The successful candidate should have a Master's degree in biomedical science, neuroscience, computer science, mathematics, physics or a related field. In particular, the applicant should demonstrate the ability to acquire relevant skills reasonably fast. They should be willing to perform experiments with human participants. Desirable qualities in candidates include intellectual curiosity, a strong background in maths, skills in programming (e.g., C#, C/C++, Python, Matlab) and signal processing and analysis. Further assets are a creative mind, good problem solving skills and a collaborative and collegial attitude.

Selected references:

1.Pozzi, N.G., et al., Freezing of gait in Parkinson's disease reflects a sudden derangement of locomotor network dynamics (2019) Brain 142(7), 2037-2050

2. Arnulfo, et al. Phase matters: A role for the subthalamic network during gait (2018) Plos ONE, 13.

3. Canessa, A., et al. Striatal dopaminergic innervation regulates subthalamic beta-oscillations and cortical-subcortical coupling during movements: Preliminary evidence in subjects with Parkinson's disease (2016) Frontiers in Human Neuroscience, 10.

Contacts: andrea.canessa@unige.it

3. The recovery of motor skills through enhancement and reorganization of sensori-motor information

Tutor: Casadio Maura

Department: https://www.dibris.unige.it/

Description: This project is based on the hypotheses that (1) in neurological diseases, in addition to motor dysfunction, somatosensory deficits induce specific and identifiable motor and neural alterations influencing the ability to perform daily living activities, and that (2) targeting motor and somatosensory deficits with highly personalized rehabilitative interventions enhances the recovery process and improves the living conditions of people suffering from these diseases.
The work has the following specific objectives (SO):

- (SO1) To develop and test new technological solutions for determining and quantifying motor and sensory deficits and the corresponding neuromuscular activation patterns together with their impact on daily life tasks. The expected outcome is a set of indicators for the subject's abilities that can be used as input parameters for the control of assistive or therapeutic devices;
- (SO2) to develop and test new low-cost sensory stimulation technologies that enable training or enhancement (i.e. 'sensory enhancement or substitution') of somatosensory abilities at home and in clinical settings. The expected deliverables are different versions of technological aids that can be used in rehabilitative settings targeting specific somatosensory modalities;
- (SO3) to define and test adaptive and highly personalized rehabilitation protocols using the results of the objectives (SO1) and (SO2).

The expected outcome is the identification of rehabilitative pathways that while following international guidelines, can also be customized according to individual disability and improvement with the aim of promoting the recovery of motor and sensory performance. If successful, this research will generate knowledge and low-cost technologies to implement at home and in the clinic effective paradigms of sensory and motor training for people suffering from neurological diseases. Furthermore, this research will broaden our understanding about the impact of sensory deficits on motor skills and on the possibility of recovering them.

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4. Visual perception and interaction in virtual and augmented reality environments

Tutor: Manuela Chessa, Fabio Solari

Department: DIBRIS (University of Genoa) www.dibris.unige.it

Description: The research theme aims, on the one hand, to devise novel paradigms to create virtual and augmented reality (VR/AR) environments, in which people can interact by exploiting their natural skills in an ecological way. In particular, actual trends take into consideration both novel wearable virtual, optical and video see through technologies, and spatial augmented reality techniques. Besides virtual visual information added to the real world, also interaction techniques and the haptic feedback play an important role to improve the sense of presence in VR/AR environments. On the other hand, the research theme aims to develop a methodology to measure the ecology of interaction in VR/AR, the perceptual and behavioral differences between interacting in real world or in VR/AR, and to understand whether VR/AR could enhance the cognitive performance (e.g. the situation and context awareness) in several fields of applications (e.g. rehabilitation or training tasks).

Requirements: Master Degree in Bioengineering, Computer Science, Computer Engineering, Robotics, equivalent degree.

References:

M. Chessa, G. Maiello, L.K. Klein, V.C. Paulun, F. Solari (2019) Grasping objects in immersive Virtual Reality. IEEE Conference on Virtual Reality and 3D User Interfaces (IEEEVR), pp. 1749-1754.

M. Chessa, G. Maiello, A. Borsari, PJ Bex (2019) The Perceptual Quality of the Oculus Rift for Immersive Virtual Reality. Human Computer Interaction, vol. 34(1), pp. 51-82.

G. Maiello, M. Chessa, F. Solari, P. J Bex (2014) Simulated disparity and peripheral blur interact during binocular fusion. Journal of Vision, July 17, 2014, 14(8)13.

Contacts: manuela.chessa@unige.it, fabio.solari@unige.it

5. PET and ASL imaging techniques in epileptic pediatric patients

Tutors: Marco Fato, Lino Nobili, Domenico Tortora

Department: DIBRIS (University of Genova), in collaboration with Advanced Neuroimaging Center, Neuroradiology Unit, IRCCS Istituto Giannina Gaslini, Genova
http://www.dibris.unige.it

Description: When standard pharmaceutical treatments fail to control seizures in epileptic patients, surgical removal of the cortical region of seizure onset is a valid alternative. Several lines of evidence links the optimal surgical outcome to the early diagnosis at pediatric age and to the accurate localization of the focal onset. This latter is performed with a series of complex electrophysiological and imaging studies that include MRI and PET acquisitions, among others. PET is a technique largely adopted in neurology that measures cellular metabolism. The most commonly used tracer is called FDG (fluorodeoxyglucose), so the test is sometimes called an FDG-PET scan. This technique has several drawbacks as it exposes children to ionizing radiations and often a general anesthesia is needed to perform the exam (with all the risks and costs connected). Moreover PET has a low spatial resolution. Given the large correlation between metabolism and blood consumption (cellular nutrients are largely transported through blood flow), a valid alternative technique to measure a secondary variable of metabolism (i.e. blood flow variations) exploits a MRI sequence called Arterial Spin Labeling. This way some benefits can be introduced at patients reducing the need of radioactive studies, increasing the spatial resolution of metabolic observations hence increasing localization power of the presurgical investigations. Only few recent studies have shown that ASL might provide useful information in the presurgical evaluation of epileptic patients, comparable to those obtained from FDG PET. However, these studies are based only on adult samples and not reporting the surgical outcome. Moreover, it is well know that cerebral blood flow and brain metabolism are strongly influenced by age, thus the above results cannot directly extended to children. Hence to date, any study exists that directly relate the role of ASL in the presurgical evaluation of epileptic children (where early diagnosis and resective surgery would be more effective) to the surgical outcome. The usage of ASL in the presurgical protocol of drug-resistant children would significantly reduce the requirement of more invasive studies. Noteworthy, we have recently compared the information obtained by FDG PET and ASL in two children with focal drug-resistant epilepsy and the results are notably encouraging showing a high level of correspondence between the two techniques. We propose a comparison study between PET and ASL imaging techniques in epileptic pediatric patients and a correlation study with high-density EEG data.
Requirements: background in bioengineering, physics, computational neuroscience, computer science. Attitude for problem solving. Interests in understanding/learning basic biology.

Reference: Proisy, et al., Diagnostic and interventional imaging, 97(2), 151-158.

Contacts: marco.fato@unige.it; domenicotortora@gaslini.org; lino.nobili@unige.it.

6. Nano-neuro interfaces for brain-on-a-chip studies

Tutor: Sergio Martinoia, Roberto Raiteri

Department: DIBRIS (University of Genova)
http://www.dibris.unige.it

Description: We are interested in investigating how computational properties emerge in 3D neuronal populations in a human brain model in which iPSC (induced Pluripotent Stem Cells) derived neurons are used. The final aim is to develop a brain-on-a-chip platform to study how information processing and transmission is related to the properties of the neuronal network. In this PhD project we propose to develop a systematic and controlled experimental approach for investigating the dynamics of 2D (as a control) and 3D neuronal networks coupled to innovative high-density sensing devices by means of nano-transducers for neuromodulation. We plan to introduce piezoelectric nanoparticles to stimulate neurons using ultrasound and gold nano-rods to inhibit neurons using IR light. The main expected technological result will be the development of a new integrated set-up with nano-tools for neuronal modulation and high-density large-scale (4Kelectrodes) for neuronal recording. This would represent a novel and automated system for *in-vitro* neuropharmacology tests and, on a longer term perspective, a tool for precision medicine. In the last part of the project we foresee to challenge our experimental models with chemical substances and to study the electrophysiological response with respect to specific parameters (biomarkers). The project will be conducted in cooperation with 3Brain company (www.3Brain.com)

Requirements: background in bioengineering, physics, computational neuroscience, computer science. Attitude for problem solving. Interests in understanding/learning basic biology.

Reference:

Rojas C., Tedesco M.T., Massobrio P., Marino A., Ciofani G., Martinoia S., and Raiteri R., Acoustic stimulation can induce a selective neural network response mediated by piezoelectric nanoparticles, J. Neural Eng., 15 (2018)

S. Yoo, S. Hong, Y. Choi, J. H. Park, and Y. Nam, "Photothermal Inhibition of Neural Activity with Near-Infrared-Sensitive Nanotransducers," ACS Nano. 2014 Aug 26;8(8):8040-9.

Tedesco M., Di Lisa D., et al., Soft chitosan microbeads scaffold for 3D functional neuronal networks, Biomaterials, 156, 159-171, (2018)

Contacts: sergio.martinoia@unige.it; roberto.raiteri@unige.it

7. Design and realization of an inkjet printed Micro Electrode Array for neurophysiological applications

Tutors: Sergio Martinoia, Andrea Spanu

Department: DIBRIS (University of Genova)
http://www.dibris.unige.it

Department: DIEE (University of Cagliari),
http://dipartimenti.unica.it/ingegneriaelettricaedelettronica

Description:
Organic Electronics has attracted considerable attention during the past years, thanks to the possibility of developing advanced electronic systems on highly flexible plastic substrates using cost-efficient fabrication technologies. In particular, organic devices and materials can be properly tailored in order to develop highly specific sensing tools that, to date, have been widely employed for the realization of different kinds of bioelectronics devices and systems.

The main idea behind this project is to employ an ink-jet device to realize an innovative, low-cost and multi-parametric organic-based sensing array. The sensors will be fabricated by using solution processable materials and possibly by inkjet or other printing approaches, with the aim of obtaining a highly flexible and low cost lab-on-chip device capable of detecting at the same time different bio-chemical cell-related inputs such as electrical activity, pH variations, temperature and other stimuli that could be of interest in the neurophysiological field.

Requirements: background on bioelectronics and material science. Interest in understanding and study the physics of devices.

Reference:
Spanu, A., Viola, F., Lai, S., Cosseddu, P., Ricci, P. C., Bonfiglio, A. (2017). A reference-less pH sensor based on an organic field effect transistor with tunable sensitivity. ORGANIC ELECTRONICS, vol. 48, p. 188-193, ISSN: 1566-1199

A. Spanu, S. Lai, P. Cosseddu, M. Tedesco, S. Martinoia, A. Bonifglio "An organic transistor-based system for reference-less electrophysiological monitoring of excitable cells" Sc. Reports 5, 8807, 2015

Contacts: sergio.martinoia@unige.it; andrea.spanu@unica.it;

8. Recreating in vitro interconnected brain regions coupled to Multi-Electrode Arrays: towards a brain-on-a-chip

Tutor: Paolo Massobrio

Department: DIBRIS (University of Genova)

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Description: The brain is a complex system characterized by the presence of different neuronal populations (e.g., cortical, hippocampal, thalamic neurons) which interact following well-defined principles of connectivity [1]. Nonetheless, brain is truly three-dimensional (3D), and such a spatial organization deeply influences the emergent electrophysiological activity [2]. This PhD project will combine Multi-Electrode Array (MEA) technology with ad hoc techniques (patterning, microfluidics) to engineer neuronal networks for coupling different neuronal populations (in a 3D fashion) to a MEA with the aim to recreate interconnected brain-regions-on-a-chip. Since the complexity of the brain, the use of simplified *in vitro* experimental models is a strategic choice to understand more in details the relationships between connectivity and dynamics, as well as to provide insights to understand pathologies which damage the interactions among neuronal populations (e.g., Parkinson disease which involves the cortical-thalamic circuit). During this 3-years project, the PhD student will be involved both in experimental (choice of the strategy to interconnect neuronal populations, experimental recordings) and computational (development of algorithms to explore the emergent dynamics and the functional topological properties) aspects.

Requirements: background in bioengineering, computational neuroscience, computer science. Interests in understanding/learning basic biology. High level of proficiency of Matlab and/or Python is required.

References:

[1] T. T. Kanagasabapathi et al., "Functional connectivity and dynamics of cortical-thalamic networks co-cultured in a dual compartment device," *Journal of Neural Engineering*, vol. 9, no. 3, 2012, Art. no. 036010.

[2] M. Frega, M. Tedesco, P. Massobrio, M. Pesce, and S. Martinoia, "Network dynamics of 3D engineered neuronal cultures: a new experimental model for in-vitro electrophysiology," *Scientific Reports*, vol. 4, no. 5489, 2014.

Contacts: paolo.massobrio@unige.it

9. New tools to decode the mechanisms underlying corticomuscular coherence

Tutor: Luca Mesin
Department: Electronics and Telecommunications, Politecnico di Torino, Turin, Italy
http://www.det.polito.it/research/research_areas/electronic_bioengineering/mathematical_biology_and_physiology

Description: The interaction between central nervous system and muscles may be studied by a joint acquisition of electroencephalogram (EEG) and surface electromyogram (EMG). In fact, by means of finding similarity patterns between EEG and EMG signals (corticomuscular coherence), pathways of functional connections can be investigated under physiological conditions (e.g., neural synchrony has been suggested as mechanism for integrating distributed sensorimotor systems involved in coordinated movements and muscle synergies [1]) and when they result compromised by a pathology (e.g., after a stroke [2]).

Preliminary simulation and processing tools are available and will be improved during the proposed doctoral study. Specifically, the PhD student will be involved in the following activities.

1. Simulation of motor neurons pools and EMG response of the innervated motor units (MU).

2. Implementation of experimental protocols (using commercial EEG systems and advanced EMG amplifiers developed by LISiN group, in Turin).

3. Development, implementation and test of methods to estimate corticomuscular coherence/synchronization.

An example of application concerns the control of human standing posture. In this case, the coherence between EEG and MUs rate coding (extracted by decomposition algorithm and reflecting the synaptic drive to motor neurons) will be investigated to address the question of whether the corrections to postural sways are triggered internally or externally [3].

Requirements: The research context is a branching field of Neuroscience and it spreads its foundations throughout a variety of disciplines, e.g., mathematics and its applications, computer science, medicine, physiology, physics and psychology. The main skills required by the candidate concern modelling, signal processing and implementation in Matlab of new algorithms.

References:
[1] de Vries IE, et al.,. J Neurophysiol. 2016;116:2576-85.
[2] Mima T, et al., Stroke. 2001;32(11):2597-601.
[3] Bottaro A, et al.,, Hum. Mov. Sci. 2008;27:473–495.

Contacts: luca.mesin@polito.it

10. Injectable hydrogels for neuroengineering

Tutor:
Laura Pastorino
Sergio Martinoia

Department:
DIBRIS, University of Genova
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Description:
The proposed theme of research concerns the design, fabrication and characterization of injectable hydrogels able to sustain neuronal cell adhesion, differentiation and network formation. The possibility to impart specific properties to the systems, e.g. by the inclusion of gold nanoparticles, graphene or graphene oxide, will be also evaluated. To this aim, biopolymeric hydrogels will be developed and characterized respect to their inner morphology, mechanical properties and bioactivity. The multicomposite systems will be characterized and tested in vitro by using primary neuronal cells and neurons differentiated from induced human pluripotent stem cells. Finally the developed hydrogels will be tested for their use as bio-inks for 3D printing of complex tissue models.

Requirements:
background in bioengineering, materials science, chemistry, physics or related disciplines. Attitude for problem solving. Interests in experimental work in the lab.

References:
- Tedesco, Maria Teresa, et al. "Soft chitosan microbeads scaffold for 3D functional neuronal networks." Biomaterials 156 (2018): 159-171.
- Haring, Alexander P., et al. "Process-and bio-inspired hydrogels for 3D bioprinting of soft free-standing neural and glial tissues." Biofabrication 11.2 (2019): 025009.

Contacts:
Email: laura.pastorino@unige.it

11. Mechanobiology of arrhythmia

Tutors: Roberto Raiteri

Department: DIBRIS (University of Genova)
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Description:
The project aims at investigating electoral and mechanical properties of cells *in vitro*, how such properties influence each other and how they are associated with disease or dysfunction. This would allow a better understanding of the mechanisms of pathogenesis or dysfunction progression, as well as novel disease treatment strategies.
The candidate will focus on the relation between cytoskeleton structure/function of cardiac muscle cells and arrhythmia, a set of heart dysfunctions that can cause sudden cardiac arrest and stroke. The study will be conducted experimentally at the single cell level by integrating different experimental techniques, including atomic force microscopy, optical microscopy, and electrophysiology recording. The candidate is expected to develop new *in vitro* experimental methods and data analysis techniques for the electromechanical characterization of cardiac myocites.

Requirements:
The ideal candidate holds a Master degree in electronic engineering, bioengineering or biophysics and has some practical experience in one or more of the following areas: design of analog electronic circuits, electrophysiology, soft matter mechanical testing. She/he should also be interested in the development of new experimental set-ups.

References:
JF. Saenz Cogollo *et al.* “A new integrated system combining atomic force microscopy and micro-electrode array for measuring the mechanical properties of living cardiac myocytes” *Biomed. Microdevices*, **2011** 13(4), 613-21

J.P. Kerr *et al.* “Detyrosinated microtubules modulate mechanotransduction in heart and skeletal muscle” *Nature Communications* **2015** 6: 8526 doi:10.1038/ncomms9526

G. Caluori *et al.* “Non-invasive electromechanical cell-based biosensors for improved investigation of 3D cardiac models Biosensors and Bioelectronics”, *Biosensors and Bioelectronics* **2019** 124, 129-135

Contacts: roberto.raiteri@unige.it

12. Perceptual and motor issues in the development of interactive intelligence

Tutor: Silvio P. Sabatini

Department: DIBRIS (University of Genoa)
http://www.pspc.unige.it

Description: Interaction is an essential paradigm, not only to understand the purpose of an intelligent system (in a closed loop with the external environment), but also to formalize and solve, from a computational point of view, the problem of the collection and organization of sensory data, according to efficiency and efficacy criteria. Human perception intrinsically originates from a (physical) interaction process between a neurosensory system and the external environment. Such an interaction allows us to gain sensations about the world's physical properties, and allows a flexible development of the brain's specific functionalities. A proper concurrent refinement of sensory and motor capabilities is crucial for a systemic development of natural and artificial intelligence.
Within this framework, a PhD research project is available on the following specific theme:
Human perception and sensorimotor skills in normal and pathological conditions.
The goal is to define models for understanding and measuring sensory and sensorimotor integration in the developmental age and in the elderly , in order to eventually design and validate systems, tools, and procedures for the diagnosis, re-education, conditioning and therapy of disorders associated to pathologies or neurological damage.
The project will provide the opportunity to work on neural modeling, visual psychophysics, robotics, or a combination of them. Experimental, modeling, and theoretical approaches might be pursued with a different accent according to personal attitude.

Requirements: background in bioengineering, computer science, physics or related disciplines. Attitude for problem solving.

References:

1. « Information Theory And Sensory Perception» https://www.witpress.com/elibrary/wit-transactions-on-state-of-the-art-in-science-and-engineering/27/18518
2. Marco Boi, Martina Poletti, Jonathan D Victor, and Michele Rucci. Consequences of the oculomotor cycle for the dynamics of perception. *Current Biology*, 27(9):1268–1277, 2017.
3. Giulia Sedda, David J. Ostry, Vittorio Sanguineti, and Silvio P. Sabatini. Engaging motor training disambiguates perception of complex visual stimuli. *Submitted,* 2020.

Contacts: silvio.sabatini@unige.it

13. Dynamic tumor modeling

Tutors: Marco Fato, Silvia Scaglione

Description: The goal besides this work is to analyze cancer cells response to traditional or immune-based cancer therapies in 3D advanced in vitro systems, aimed at reproducing the vascularized microenvironment typical of solid tumors.
The effects of different compounds will be tested in a dynamic environment aimed at mimic the physiological bloodstream, by using bioreactors, which can reproduce multiple flow directions, affecting the behavior of tumorigenic cells, embedded in a 3D hydrogel representing the tumor.
The student will focus on i) the computational fluid-dynamic simulations (CFD) of the fluid motion within the bioreactor and the drug/mass transport kinetic within the circuit and the 3D tumor model, respectively, ii) the fabrication of the bioreactor system through 3D printing technology, iii) the process of 3D tumor realization (gel manufacturing and cells culture), iv) the analysis of cancer cells response. The work will be constituted also by microscopy analysis (optical microscopy and fluorescence confocal microscopy) and consequent images post-production and data analysis (ImageJ).

Requirements: The ideal candidate holds a Master degree in bioengineering, chemical engineering, biotechnology and has some practical experience in one or more of the following areas: CFD, 3D printing, hydrogel processing, cell biology.

References:

Marrella, Alessandra, et al. "Cell-laden hydrogel as a clinical-relevant 3D model for analyzing neuroblastoma growth, immunophenotype and susceptibility to therapies." *Frontiers in immunology* 10 (2019): 1876
Cavo, Marta, et al. "Microenvironment complexity and matrix stiffness regulate breast cancer cell activity in a 3D in vitro model." *Scientific Reports* 6 (2016): 35367.

14. Critical dynamics in the human brain

Tutor: Arnulfo Gabriele

Department: DIBRIS www.dibris.unige.it

Description: The human brain has been hypothesized to operate akin to a critical process. Neuronal avalanches, an hallmark of such systems, are characterised by activity cascades that exhibit power-law size distributions and has been investigated in “in vitro”, “in vivo”, and human invasive, and noninvasive electrophysiological recordings. A large body of literature is currently investigating the basis of consciousness defined as the capacity of the brain to integrate (sensory) information. It known that systems poised at their critical states are in the optimal conditions to perform such task. On the other hand, the capacity of integrate, memorise information largely happens during sleep. Not much is known about the transitions between critical states across vigilance states. Some lines of evidence support the hypothesis of a breakdown in brain criticality during unconscious states such as the non-REM sleep, and also coma. An observation of deviations from the critical state for certain vigilance states would also imply phase transitions between vigilance states in the context of self-organized criticality.

In this project, the candidate will investigate the link between criticality (e.g. avalanches propagation) and connectivity during different sleep stages as well as in the transition between those. A better understanding of these properties could support existing theories of consciousness by providing evidence of theorised mechanisms as well as pave the way to new quantitative tools to investigate sleep and consciousness disorders.

Requirements: Bioengineering, maths, physics

References:

- Priesemann V, Valderrama M, Wibral M, Le Van Quyen M (2013) “Neuronal Avalanches Differ from Wakefulness to Deep Sleep – Evidence from Intracranial Depth Recordings in Humans”. PLOS Computational Biology.
- Palva JM, Zhigalov A, Hirvonen J, Korhonen O, Linkenkaer-Hansen K, Palva S (2013) “Neuronal long-range temporal correlations and avalanche dynamics are correlated with behavioral scaling laws”. Proc Natl Acad Sci U S A 110:3585–3590.
- Zhigalov A, Arnulfo G, Nobili L, Palva S, Palva JM (2015) “Relationship of Fast- and Slow-Timescale Neuronal Dynamics in Human MEG and SEEG”. The Journal of Neuroscience, April 1, 2015 • 35(13):5385–5396 • 5385.

Contacts: gabriele.arnulfo@unige.it

15. Electrophysiological Correlates of Neurorehabilitation

Tutor: Michela Chiappalone, Marianna Semprini

Department: Rehab Technologies (Istituto Italiano di Tecnologia), http://rehab.iit.it/

Description: To evaluate the effects of a neurorehabilitation therapy [1], in addition to the classic clinical scales, several metrics based on electrophysiological measurements are advancing [2]. A critical aspect of these measurements consists in the fact that these are almost always separate measures, which capture a partial image of the recovery, for example because they describe changes either at the level of the peripheral (EMG) or central nervous system (EEG, MEG). The ultimate goal of this PhD work consists of integrating all these indicators in order to provide a global assessment of recovery, which takes into account the different facets of functional recovery. The Candidate will be requested to develop a software platform for data analysis, capable of (1) compute novel parameters derived from the functional/effective connectivity analysis of EEG (primarily) and (2) combine parameters from different electrophysiological measurements (e.g., EMG & EEG). The PhD activities will include experiments with patients and strong collaboration and interaction with our partners. To this end, the Candidate will benefit from a lively network of collaborations with hospitals and research institutions, such as Fondazione Mondino in Pavia, San Camillo Hospital in Venice, Ospedale Villa Beretta in Lecco, Fondazione Don Gnocchi in Milan. This project requires broad expertise in electrophysiology (i.e. EEG acquisitions and analysis) and a demonstrated expertise in electronic engineering and software development. The ideal candidate should hold a degree in electronic/biomedical engineering or related disciplines, be a highly motivated and creative individual who wants to work in a dynamic, multi-disciplinary research environment. Former lab experience and previous technical and scientific results will be highly considered.

Requirements: Background in bioengineering; proficient programming skills: experience with Matlab/Simulink, C and/or Python for data analysis. Experience with human acquisitions with EEG/hdEEG. Experience in clinical environment will be taken in high account.

References:

[1] Semprini, M., Laffranchi, M., Sanguineti, V., Avanzino, L., De Icco, R., De Michieli, L., & Chiappalone, M. (2018). Technological approaches for neurorehabilitation: from robotic devices to brain stimulation and beyond. *Frontiers in Neurology*, *9*, 212.

[2] Iandolo, R., Marini, F., Semprini, M., Laffranchi, M., Mugnosso, M., Cherif, A., De Michieli, L., Chiappalone, M., and Zenzeri, J. (2019). Perspectives and Challenges in Robotic Neurorehabilitation. *Applied Sciences*, 9(15), 3183.

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