PhD Program in Bioengineering and Robotics

Curriculum: Bioengineering

Research themes

NEUROPHYSIOLOGICAL CORRELATES OF SLEEP DISRUPTION ACROSS BRAIN DISORDERS
ECOLOGICAL VIRTUAL REALITY FOR ASSESSMENT AND REHABILITATION IN SENSORY, MOTOR, AND COGNITIVE DISABILITIES
BUILDING DIGITAL TWINS FROM IMAGING AND ELECTROPHYSIOLOGICAL DATA TO TEST ELECTROCEUTICAL STRATEGIES
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DEVELOPMENT AND CHARACTERIZATION OF NOVEL ELECTRO-MECHANICAL STIMULATION STRATEGIES FOR <i>IN VITRO</i> APPLICATIONS
PERCEPTUAL AND MOTOR ISSUES IN THE DEVELOPMENT OF INTERACTIVE INTELLIGENCE
PATIENT DIGITAL TWINS AND ROBOTIC AGENTS TO UNDERSTAND NEUROMOTOR IMPAIRMENT AND TO PROMOTE RECOVERY
MULTIMODAL MARKERLESS MOTION ANALYSIS FOR HOME-BASED REHABILITATION
PATHWAYS FOR SELF-ENHANCEMENT: COMPARING SUPERNUMERARY TECHNOLOGIES AND COLLABORATIVE APPROACHES
OPTIMIZATION AND VALIDATION OF MARKER-LESS SYSTEMS FOR HUMAN MOVEMENT ANALYSIS
OPTIMIZATION AND CLINICAL ASSESSMENT OF HIGH-TECH SOLUTIONS FOR NEUROREHABILITATION
HUMAN BRAIN-ON-CHIP MODELS FOR NEURO-GENETIC DISEASES

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.

Neurophysiological Correlates of Sleep Disruption Across Brain Disorders

Tutors: Arnulfo Gabriele, Nobili Lino

Tutors Affiliation: DIBRIS, UNIGE, dibris.unige.it

Project Description

Humans spend a significant portion of their lives asleep. Sleep is essential for maintaining homeostasis, supporting synaptic pruning and neuronal plasticity, and consolidating memory. Disruptions to sleep can have profound and varied impacts on brain function and development across the lifespan.

In early childhood, chronic sleep loss, difficulty falling asleep, and frequent night awakenings have been linked to neuronal loss, cognitive and behavioral impairments, and even serve as early predictors of neurodevelopmental disorders such as autism spectrum disorder. For example, one study found that the sleep–wake rhythm at age one could predict an ASD diagnosis with 76.9% accuracy. In adolescence, insufficient or fragmented sleep has been associated with abnormal development of the prefrontal cortex, potentially impairing executive function and mental health. In individuals with attention deficit hyperactivity disorder (ADHD), sleep problems are known to worsen daytime symptoms. Furthermore, persistent sleep difficulties in preterm infants and other pediatric populations may contribute to long-term impairments in cognitive, behavioral, and motor function.

Sleep disruption is also intricately linked to neurodegenerative diseases. There is a wellestablished bidirectional relationship between sleep and neurodegeneration: not only do sleep abnormalities frequently appear early in the disease course, but they may also actively contribute to the progression of pathology. Disrupted sleep is associated with increased oxidative stress and the accumulation of misfolded proteins—both hallmarks of neurodegeneration. The glymphatic system, which facilitates the clearance of neurotoxic waste during sleep, is thought to play a key role in this process. Sleep disturbances are common in disorders such as Alzheimer's, Parkinson's, and Huntington's disease, and understanding these disruptions may offer insights into early diagnosis and diseasemodifying interventions.

This PhD project aims to investigate the neurophysiological correlates of sleep disruption across a spectrum of brain disorders, including neurodevelopmental, neurological, and neurodegenerative conditions. By leveraging electrophysiological recordings across different stages of pathology and vigilance states, the project will seek to characterize maladaptive modulations in brain dynamics associated with disordered sleep.

The successful candidate will join a multidisciplinary research environment and work in close collaboration with IRCCS Gaslini Hospital, a leading center for pediatric neurology and neurodevelopmental care. This project offers the opportunity to contribute to clinically meaningful research at the intersection of sleep, brain development, and neurodegeneration.

This PhD project offers comprehensive training in advanced neurophysiological methods and integrative neuroscience. The candidate will develop expertise in the acquisition and analysis of electrophysiological signals, including high-density EEG, polysomnography, and intracranial recordings where available. Training will focus on characterizing brain network dynamics across different vigilance states and disease stages, with particular emphasis on sleep-specific biomarkers and signal features such as oscillatory patterns, cross-frequency coupling, and functional connectivity.

The student will be introduced to a range of analytical frameworks, including timefrequency decomposition, phase-amplitude coupling metrics, machine learning-based classification, and statistical modeling of brain dynamics. Emphasis will be placed on linking physiological findings to clinical phenotypes in both pediatric and adult populations. The project is inherently interdisciplinary and the candidate will gain exposure to the translational aspects of neuroscience research, including the interpretation of findings in a clinical context and the formulation of research questions with direct patient relevance. **Required Skills:**

- Strong background in neuroscience, biomedical engineering, or a related field
- Solid foundation in signal processing and statistical analysis
- Programming proficiency in Python, MATLAB, or similar languages used in neuroscience research
- Interest in sleep physiology, brain network analysis, and clinical applications
- Excellent communication skills and the ability to work in a multidisciplinary team

• Previous experience with EEG or neuroimaging data is desirable but not mandatory **Contacts**: gabriele.arnulfo@unige.it

Ecological Virtual Reality for Assessment and Rehabilitation in Sensory, Motor, and Cognitive Disabilities

Tutors: Andrea Canessa, Silvio Sabatini

Tutors Affiliation: DIBRIS, University of Genoa

Project Description

Traditional assessment and rehabilitation methodologies often have inherent limitations due to their artificial and highly controlled nature, making them significantly distant from the complexity and variability of situations encountered by individuals with disabilities in everyday life. This gap between clinical environments and real-world scenarios can limit the generalization of learned skills, consequently reducing the effectiveness of rehabilitation interventions. It is thus essential to develop innovative tools that allow clinicians and researchers to move beyond laboratory settings, bringing assessment and rehabilitation approaches closer to real-life conditions.

In this context, Virtual Reality (VR) emerges as a key technology due to its capability to create immersive, ecologically valid, and highly interactive environments. VR enables realistic simulations of daily life situations, allowing patients to face concrete challenges, learn adaptive strategies, and manage difficult scenarios within a safe yet realistically immersive environment.

This doctoral theme aims to explore the potential of VR for functional assessment and rehabilitation, focusing specifically on three main disability categories:

- **Motor Disabilities**: For patients with neurodegenerative diseases such as Parkinson's disease or multiple sclerosis, immersive scenarios will enable them to tackle complex motor tasks like navigating crowded environments, managing unexpected obstacles, or safely crossing busy streets.
- **Sensory Disorders**: For individuals experiencing hearing loss or visual deficits, interactive virtual environments will simulate realistic sensory challenges, such as background noise or visually complex scenes, enhancing their ability to adapt and improve autonomy in real-world settings.
- **Cognitive Disorders**: In cases of cognitive disabilities associated with neurodevelopmental conditions (e.g., autism or ADHD), tailored scenarios will be developed to specifically stimulate attention, executive functions, and planning skills, as well as to manage stress in everyday situations.

Additionally, the project will investigate the integration of generative Artificial Intelligence (AI) models within VR environments to further enhance realism and interactivity. This approach aims to create highly customizable and dynamically adaptable virtual experiences tailored to individual user needs.

The main activities of the doctoral project will include:

- Designing and implementing realistic and interactive scenarios with multisensory feedback;
- Integrating and validating generative AI models to enhance immersive scenarios;
- Conducting clinical studies to validate the effectiveness of the developed approaches, comparing them with traditional techniques;
- Developing novel analytical methodologies to interpret collected data and optimize the transferability of rehabilitation skills acquired into everyday life.

The doctoral candidate will acquire advanced interdisciplinary skills, working at the intersection of bioengineering, neuroscience, psychology, and Artificial Intelligence, significantly contributing to technological innovations that concretely improve the quality of life and autonomy of individuals with disabilities.

Requirements:

The successful candidate should have a Master's degree in biomedical science, neuroscience, computer science, psychology, 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, 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.

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Building Digital Twins from Imaging and Electrophysiological Data to Test Electroceutical Strategies

Tutors: Marco Fato, Federico Barban

Tutors Affiliation: Dipartimento di Informatica, Bioingegneria, Robotica e Ingegneria dei Sistemi (DIBRIS), Università degli Studi di Genova

Project Description

Neurological conditions such as stroke and traumatic brain injury (TBI) frequently lead to long-lasting impairments in movement and sensation, often resistant to conventional pharmacological treatments and rehabilitation. This research project is part of a broader initiative aimed at promoting recovery through neurostimulation techniques. The focus is on developing a "digital twin"—a computational model that mimics brain dynamics—built using multimodal neurobiological data. This model will serve as a platform to explore and optimize stimulation-based therapies before they are applied in living systems.

The digital twin will be created by integrating advanced imaging and electrophysiological recordings collected from experimental models undergoing recovery. Structural and functional brain scans will be used to assess injury and monitor changes in connectivity over time. Simultaneously, high-resolution electrical activity from key brain regions will be recorded to capture detailed neural dynamics during the recovery process. These data, combined with behavioral and connectivity measures, will be analyzed using dedicated computational pipelines.

The ultimate goal is to construct biologically informed, dynamic models that emulate the injured brain's structure and function. These models will offer a valuable tool for simulating and tailoring therapeutic strategies, ultimately supporting more precise and effective neurostimulation-based interventions.

Requirements: Applicants should have a background in bioengineering, neuroscience, computer science, or a related field. Proficiency in programming languages such as Python and Matlab is essential. Experience with electrophysiological data analysis, imaging dta analysis, modeling and neuromorphic engineering is highly desirable. Familiarity with machine learning techniques, and real-time computing is a plus.

References

[1] Angotzi, G. N., et al. (2019). SiNAPS: An implantable active pixel sensor CMOS-probe for simultaneous large-scale neural recordings. Biosensors and Bioelectronics, 126, 355-364.

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Tools for connecting to health information systems for the reuse of clinical data for research purposes

Tutors: Prof. Mauro Giacomini

Tutors Affiliation: University of Genova

Project Description

The second-generation electronic health record is being developed throughout Italy, characterized by overcoming the purely documentary vision to make available analytically analyzable data. Similar efforts are being implemented at European level for the creation of the European Health Data Space.

Specific objectives of the doctorate could be:

- Design, implementation and testing of clinical data anonymization tools
- Design, implementation and testing of pipelines, based on natural language processing methods, for the extraction of analytical data from natural language texts, appropriately anonymized with the tools made available in the previous point.
- Identification, development and testing of methods based on artificial intelligence to answer questions of strong clinical interest.

During the doctorate, appropriate case studies will be identified within which the tools described in the previous points will be tested, the validity of which will be assessed with groups of doctors interested in the study.

Requirements:

- STEM master degree;
- Knowledge of at least one of the main programming languages and basic knowledge of the related frameworks for Artificial Intelligence;
- Languages: Italian and English.

References:

D. Stojanov, E. Lazarova, E. Veljkova, P. Rubartelli, M. Giacomini "Predicting the outcome of heart failure against chronicischemic heart disease in elderly population – machine learning approach based on logistic regression, case to Villa Scassi hospital Genoa, Italy" Journal of King Saud University – Science, 2023, vol. 35, Issue 3, pp, 1-12, Id. 102573, doi: <u>https://doi.org/10.1016/j.jksus.2023.102573</u>

S. Mora, D. R. Giacobbe, C. Bartalucci, G. Viglietti, M. Mikulska, A. Vena, L. Ball, C. Robba, A. Cappello, D. Battaglini, I. Brunetti, P. Pelosi, M. Bassetti, M. Giacomini "Towards the automatic calculation of the EQUAL Candida Score: extraction of CVC-related information from EMRs of critically ill patients with candidemia in Intensive Care Units" Journal of Biomedical Informatics, 2024 doi: https://doi.org/10.1016/j.jbi.2024.104667

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Biological and Digital brain twin: computational models and in vitro neuronal networks

Tutors: Sergio Martinoia

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Project Description: The human brain remains one of the most profound frontiers in science. Understanding its intricate functions and addressing its disorders pose significant challenges. This project aims at developing an advanced pipeline for multichannel data analysis, encompassing a broad range of electrode arrays from tens to thousands of channels. This pipeline will be capable of handling complex datasets generated from both 2D and 3D neural networks, as well as in vitro organoids. In vitro cultures are prepared from human-derived induced-pluripotent stem cells (h-iPSCs).

The primary objectives of this PhD project consist of **1**) creating a versatile and scalable system that can efficiently process and analyze large volumes of electrophysiological data starting from a pipeline already available in the lab (i.e. SpyCode [1]) and **2**) identifying electrophysiological 'biomarkers' that can help in distinguishing between healthy and pathological neural and brain networks. **3**) Implement computational models capable of reproducing the intrinsic network activities supporting the data analysis and biomarker's identifications. These biomarkers might be based on connectivity, spike/burst-related metrics as well as complexity metrics and network dynamics based measures, will inform the development of online therapeutic electroceutical strategies.

By advancing the capabilities of multichannel data analysis and computational models, this project aims to significantly contribute to the understanding and manipulation of complex neural networks. The outcomes of this research have the potential to impact various fields, including neuroscience, bioengineering, and pharmacology, by providing robust tools for the study and control of neural activity.

Requirements: Applicants are expected to have a background in (bio)engineering or mathematics or computer science; proficient programming skills: experience with Matlab, C and/or Python for data analysis. Experience on data analysis of neural signals (MUA or LFP recordings) is recommended. Previous Lab experience is a plus.

References:

[1] Bologna, L. L., et al. (2010). Investigating neuronal activity by SPYCODE multi-channel data analyzer. Neural Networks, 23(6), 685-697.

[2] Doorn N. et al. (2024). Breaking the burst: Unveiling mechanisms behind fragmented network bursts in patient-derived neurons. Stem cell report, 19-11, 1583.1597

[3] Parodi, G., et al. (2024) Electrical and chemical modulation of homogeneous and heterogeneous human-iPSCs-derived neuronal networks on high density arrays. Front. Mol. Neurosci., 17

Brain Sciences, 12(11), 1578.

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Assembling building blocks of the brain to explore the computational properties of complex *in vitro* structures coupled to Multi-Electrode Arrays

Tutors: Paolo Massobrio, Martina Brofiga

Tutors Affiliation: Dipartimento di Informatica, Bioingegneria, Robotica e Ingegneria dei Sistemi (DIBRIS), Università di Genova

Project 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, 2]. Nonetheless, brain is truly three-dimensional (3D), and such a spatial organization deeply influences the emergent electrophysiological activity [3]. 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 that can be considered the building blocks of more complex structures. 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 different neurospheroids, imaging characterization, experimental recordings) and computational (development of algorithms to explore the emergent dynamics and the functional topological properties) aspects. During the last year of the project, the candidate will characterize such structures by delivering patterns of electrical stimulation to study how the different involved neuronal populations modulate the I/O function.

Requirements: background in bioengineering, computational neuroscience, and statistics. **References**:

[1] M. Brofiga, M. Pisano, F. Callegari, P. Massobrio, Exploring the contribution of thalamic and hippocampal input on cortical dynamics in a brain-on-a-chip model, *IEEE Trans. Med. Rob. Bion.*, 2021.

[2] M. Brofiga, M. Pisano, M. Tedesco, A. Boccaccio, P. Massobrio. Functional inhibitory connections modulate the electrophysiological activity patterns of cortical-hippocampal ensembles, *Cerebral Cortex*, 2022.

[3] M. Brofiga, F. Callegari, L, Cerutti, M. Tedesco, P. Massobrio, Cortical, striatal, and thalamic populations self-organize into a functionally connected circuit with long-term memory properties *Bios. & Bioel.*, 2025.

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Dynamic modelling of cortical folding through bioprinted 4D constructs: exploration of meccano-cellular interactions in neurodevelopment

Tutors: Laura Pastorino, Donatella Di Lisa

Tutors Affiliation: Department of Informatics, Bioengineering, Robotics and Systems Engineering (DIBRIS), University of Genova

Project Description

Cortical folding is a distinctive feature of human brain development and is essential for the formation of functional neural circuits. Understanding the biomechanical and cellular dynamics underlying this process is crucial for uncovering the mechanisms of many neurodevelopmental and neurological disorders. Despite advances in computational models and biomaterial-based approaches, integrated knowledge of mechanical forces and cellular behaviors remains limited. Recent innovations, such as brain organoids-on-achip, have provided new insights but still fall short in replicating the full complexity and dynamism of cortical folding. In this context, 4D bioprinting and Al-guided smart material design offer unprecedented opportunities to recreate dynamic, physiologically relevant tissue environments. The proposed project will focus on the design and fabrication of multilayered 4D scaffolds that closely mimic the dynamic architecture of the developing human cortex. To achieve this, we will employ AI-guided design of smart materials, particularly thermo- and mechano-responsive hydrogels, capable of undergoing controlled, stimulus-induced deformations. These materials will be engineered into microscale architectures that replicate the laminar organization characteristic of cortical tissue, allowing for spatial patterning of mechanical properties and cellular distribution. External mechanical and chemical stimuli will be applied in a controlled manner to guide tissue development and induce morphogenetic processes, including cortical folding. То characterize and interpret the evolving tissue structures, a comprehensive dynamic and functional analysis will be performed. This will include real-time monitoring through advanced live-cell microscopy, 3D imaging modalities, and electrophysiological recordings to assess both structural and functional maturation of the constructs. Finally, automated data analysis will be conducted using machine learning algorithms to detect and quantify correlations between folding-related mechanical forces and cellular behaviors over time, enabling predictive modeling of neurodevelopmental trajectories.

Requirements: Applicants are expected possess a background in bioengineering/materials science/related disciplines. Attitude for experimental and computational.

References:

- 1. Gu, Qi, et al. "Functional 3D neural mini-tissues from printed gel-based bioink and human neural stem cells." *Advanced healthcare materials* 5.12 (2016): 1429-1438.
- 2. Esworthy, Timothy J., et al. "Advanced 4D-bioprinting technologies for brain tissue modeling and study." *International journal of smart and nano materials* 10.3 (2019): 177-204.
- 3. Soykan, Merve Nur, et al. "Four-Dimensional Printing Technology at the Frontier of Advanced Modeling and Applications in Brain Tissue Engineering." *Journal of Medical Innovation and Technology* 3.2 (2021): 46-57.

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Development and characterization of novel electro-mechanical stimulation strategies for *in vitro* applications

Tutors: Roberto Raiteri

Tutors Affiliation: DIBRIS, University of Genova

Project Description

Recent advances in nanomaterials and biomedical ultrasound have enabled novel strategies for remote, non-invasive cellular stimulation [1]. This research proposes the development and characterization of innovative stimulation techniques based on the synergistic use of low-intensity ultrasound and piezoelectric nanoparticles (e.g., BaTiO₃). The core objective is to establish a platform capable of precise and tunable activation of cellular processes in vitro, exploiting the mechanical-to-electrical transduction properties of nanoparticles to convert acoustic waves into localized bioelectric stimuli.

The project will explore the application of this approach in four distinct yet interconnected areas: (a) neuromodulation of neuronal cultures, aiming at controlled excitation or inhibition of neural activity [2]; (b) modulation of neuroinflammatory responses through glial cell stimulation; (c) pacing of cardiomyocytes with spatiotemporal precision; and (d) guidance of stem cell differentiation via localized electromechanical cues. A multidisciplinary methodology will be adopted, integrating nanoparticle functionalization, acoustic field optimization, electrophysiological recordings, and molecular biology techniques.

This research holds promise for the development of non-invasive interfaces for tissue engineering and regenerative medicine, paving the way for next-generation bioelectronic systems and therapeutic platforms. The proposed study will also contribute to fundamental understanding of mechanoelectrical transduction at the cell-nanomaterial interface.

Requirements: attitude toward experimental work involving the development of new setups and procedures.

References:

[1] A. Cafarelli et al., "Piezoelectric Nanomaterials Activated by Ultrasound: The Pathway from Discovery to Future Clinical Adoption," *ACS Nano* (2021) doi: 10.1021/ACSNANO.1C03087

[2] C. Rojas et al. "Acoustic stimulation can induce a selective neural network response mediated by piezoelectric nanoparticles" *J Neural Eng.* (2018) doi: 10.1088/1741-2552/aaa140

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Perceptual and motor issues in the development of interactive intelligence

Tutor: Silvio P. Sabatini

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

Project 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» <u>https://www.witpress.com/elibrary/wit-transactions-on-state-of-the-art-in-science-and-engineering/27/18518</u>
- 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. Sedda G, Ostry DJ, Sanguineti V, Sabatini SP. Self-operated stimuli improve subsequent visual motion integration. J Vis. 2021 Sep 1;21(10):13. doi: 10.1167/jov.21.10.13. PMID: 34529006; PMCID: PMC8447044.

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Patient digital twins and robotic agents to understand neuromotor impairment and to promote recovery

Tutors: Vittorio Sanguineti, Cecilia De Vicariis **Tutors Affiliation:** DIBRIS, University of Genoa, dibris.unige.it

Project Description:

Sensorimotor impairment after a stroke typically affects fine control (dexterity), strength and spinal reflexes (spasticity) [1]. Neuromotor recovery after stroke is the effect of at least two distinct phenomena. Stroke survivors may learn to move a different way than it was done before stroke (compensation). They may also relearn to move as they did before stroke. This is referred as 'restitution' or 'true recovery' and implies the restoration of the damaged cortico-spinal pathways. Upper limb neurorehabilitation after stroke typically relies on high-dose, task-oriented training of the impaired arm. Robot-mediated interventions (eg weight support, assisted movements) have been moderately successful in facilitating recovery, but are believed to mostly promote compensation rather than true recovery.

The overall goals of this research are (i) to design and test in a clinically relevant scenario new methodologies to characterize the processes involved in neuromotor recovery, and the way they affect dexterity, strength and spasticity, and (ii) to devise new technology-assisted approaches to promote true recovery.

Research to address these objectives will specifically aim at novel analytical tools involving realistic models of musculoskeletal biomechanics and neural control, including sensorimotor impairment and its associated recovery processes [2]. These models will constitute a multi-level description of the patient's body anatomy, neural control and cognitive state – a patient digital twin (PDT). PDTs will serve as basis for both impairment characterization and for technology-assisted training that is based on joint action and game theory [3].

Depending on personal attitudes and interests, research work might include (i) PDT design and characterization, including the development of techniques for model personalization to individual anatomy, size, strength, type and degree of impairment; (ii) the development of novel model-based metrics to track the temporal evolution and the mechanisms underlying compensation and true recovery; and (iii) the design a novel robot-assisted training modalities that facilitate and speed up true recovery.

Requirements: Background in biomedical engineering and/or robotics; Interest in the neural control of movements, musculoskeletal biomechanics, computational motor control, and rehabilitation technologies.

References:

[1] Krakauer, JW and Carmichael, ST. Broken Movement. MIT Press, 2017.

[2] Valero-Cuevas, F.J., Finley, J., Orsborn, A. et al. NSF DARE—Transforming modeling in neuro-rehabilitation: Four threads for catalyzing progress. J NeuroEngineering Rehabil 21, 46 (2024).
[3] De Vicariis C, Pusceddu G, Chackochan VT, Sanguineti V. Artificial Partners to Understand Joint Action: Representing Others to Develop Effective Coordination. IEEE Trans Neural Syst Rehabil Eng. 2022;30:1473-1482.

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Multimodal markerless motion analysis for home-based rehabilitation

Tutors: Maura Casadio, Matteo Moro **Tutors Affiliation:** DIBRIS, University of Genoa, dibris.unige.it

Project Description:

In recent years, rehabilitation has increasingly focused on the development of technologies that support objective assessment and personalized care. Among these innovations, markerless motion analysis [1], leveraging RGB and depth cameras and Aldriven pose estimation, has demonstrated strong potential in controlled, laboratory environments for tracking human movement. However, the application of such techniques in unstructured, real-world settings, particularly in patients' homes, remains limited, despite the growing demand for scalable and accessible home-based rehabilitation solutions.

This PhD project aims to bridge this gap by developing robust, non-invasive systems for quantitative, at-home analysis of motor patterns. The research will build upon markerless vision-based tracking, while also integrating audio analysis to enable a more complete, multimodal understanding of human movement, focusing also on the interaction between the individual and their environment. A key objective of the project is to systematically evaluate the performance of markerless motion capture techniques in environments that replicate real-world domestic conditions. This involves assessing the reliability, robustness, and accuracy of these methods when deployed in less-controlled settings, where factors such as lighting variability, furniture layout, and occlusions may affect tracking quality. In parallel, the research will investigate how audio signals, such as footstep timing, vocal exertion, or spoken instructions, can act as supplementary indicators of motor effort, cognitive-motor interaction, or engagement during physical tasks. These multiple sensing modalities will be combined through the design of sensor fusion frameworks, using advanced signal processing and machine learning techniques to integrate spatial, temporal, and contextual information into a coherent, interpretable assessment of user performance. The project will result in the development of a prototype model capable of real-time monitoring of daily functional activities, such as walking, sit-to-stand transitions, or object manipulation. Crucially, the system will be designed with adaptability in mind, enabling it to tailor analysis and feedback to the individual needs, goals, and progress of each user. By supporting flexible configurations and user-specific calibration, the platform will promote personalized rehabilitation pathways. Finally, the system will be validated through pilot studies involving both healthy individuals and patients undergoing rehabilitation, to assess its usability, clinical relevance, and potential for integration into remote care protocols. These studies will offer insights into how the proposed approach can contribute to long-term monitoring, early detection of motor decline, and adaptive intervention planning.

[1] Lam, Winnie WT, Yuk Ming Tang, and Kenneth NK Fong. "A systematic review of the applications of markerless motion capture (MMC) technology for clinical measurement in rehabilitation." Journal of NeuroEngineering and Rehabilitation 20.1 (2023): 57

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Pathways for self-enhancement: comparing Supernumerary technologies and collaborative approaches

Tutors: Camilla Pierella

Tutors Affiliation: DIBRIS, University of Genoa, https://dibris.unige.it/en

Project Description

Neuroscience and robotics are exploring supernumerary robotic limbs (A-SL) to augment human motor abilities. This technology can revolutionize medicine, industry, and humanenvironment interactions. A key challenge lies in designing effective control strategies and human-machine interfaces. Another question is: how does A-SL compare to augmentation through collaboration with another person (A-C)? This project aims to create a framework to disentangle the motor and cognitive mechanisms underlying A-SL and A-C. It will compare task performance, cognitive load, and subjective experience between the two augmentation approaches. It also investigates preferences for each modality and how they relate to individual personality traits.

Requirements: Attitude for experimental research,

Programming skill in Unity and Matlab are preferred

Familiarity with statistical toolbox

References:

[1] G. Dominijanni, S. Shokur, A. D'avella, T. R. Makin, D. Prattichizzo, and S. Micera, "The neural resource allocation problem when enhancing human bodies with extra robotic limbs," *Nat. Mach. Intell.*, vol. 3, no. 10, pp. 850–860, 2021, doi: 10.1038/s42256-021-00398-9.

[2] J. Eden *et al.*, "Principles of human movement augmentation and the challenges in making it a reality," *Nat. Commun.*, vol. 13, no. 1, 2022, doi: 10.1038/s41467-022-28725-7.

[3] D. Prattichizzo et al., "Human augmentation by wearable supernumerary robotic limbs:

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Optimization and validation of marker-less systems for human movement analysis

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Project Description

The project aims at optimizing video-based marker-less systems for human movement analysis and at their application and validation on healthy and pathological subjects. The project activities include the analysis of currently available video-based pose estimators, the optimization of neural network-based training algorithms for pose estimators, and the collection of datasets of video recordings of human movements related to both locomotion and upper limb functional tasks. Moreover, the validation of pose estimators will be evaluated in terms of test-retest reliability and by comparison with gold-standard stereophotogrammetry. Finally, the generalization capability of pose estimators will be assessed by training the algorithms on data from healthy subjects to reconstruct patients' movement.

The final goal is to validate the effectiveness of these approaches in various clinical fields, such as neurology, orthopedics and rehabilitation, and also their usability in non-clinical applications such as sports, ergonomics and home monitoring.

Requirements: skills on collection, processing and analysis of human movement data, working attitude in multidisciplinary team.

References:

Moro M, Marchesi G, Hesse F, Odone F, Casadio M. Markerless vs. Marker-Based Gait Analysis: A Proof of Concept Study. Sensors (Basel). 2022 Mar 4;22(5):2011.

Lencioni T, Carpinella I, Rabuffetti M, Marzegan A, Ferrarin M. Human kinematic, kinetic and EMG data during different walking and stair ascending and descending tasks. Sci Data. 2019 Dec 6;6(1):309

Zheng C, Wu W, Chen C, Yang T, Zhu S, Shen J, Kehtarnavaz N, Shah M. Deep Learning-based Human Pose Estimation: A Survey. ACM Computing Surveys. 2023; 56(1):11.

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Optimization and clinical assessment of high-tech solutions for neurorehabilitation

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Project Description

The project aims to optimize and apply high-tech solutions for the neurorehabilitation of patients with cognitive and motor impairments due to pathological conditions and agerelated frailties. Project activities include the analysis of technologies and devices currently available for neurorehabilitation, the integration of different approaches including robotics, Functional Electrical Stimulation and sensor-based exergames, and their pilot application on selected groups of patients. The assessment procedures will be targeted to analyze usability, safety and efficacy of these technologies compared to standard rehabilitation approaches and will make use of instrumented methods for movement analysis (stereofotogrammetry, dynamometric platform and EMG signal).

The final aim is to develop and validate advanced devices for the rehabilitation of locomotor impairments in severely affected patients and the implementation of motor-cognitive exercises for frail elderly, both in clinical and domestic settings.

Requirements: knowledge of technically advanced devices for rehabilitation, skills on collection, processing and analysis of human movement data, working attitude in multidisciplinary team.

References:

Seinsche J, de Bruin ED, Saibene E, Rizzo F, Carpinella I, Ferrarin M, Moza S, Ritter T, Giannouli E, A Newly Developed Exergame-Based Telerehabilitation System for Older Adults: Usability and Technology Acceptance Study, JMIR Human Factors, 2023 Dec 7; 10:e48845.

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Human brain-on-chip models for neuro-genetic diseases

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Project Description

Human brain-on-a-chip models hold the promise for personalized medicine. In fact, the advent of human induced pluripotent stem cells (hiPSCs) and neuronal differentiation protocols allowed the phenotype, molecular abnormalities, and drug responses to be investigated *in vitro* in a patient-specific manner¹.

In this project, we propose to study and ameliorate the phenotype of neuronal networks derived from hiPSCs of patients with genetic disorders by using brain-on-chip models with different architectures (i.e., 2D, 3D, random, patterned)^{1,2}. First, the candidate will extensively characterize the electrophysiological activity of the patient-derived neuronal networks. Then, the molecular abnormalities underpinning the phenotype will be investigated, also with the use of digital network twins³. Finally, drug testing targeting the molecular abnormalities will be performed to ameliorate the phenotype exhibited by the patient-derived neuronal networks.

Requirements: background in bioengineering, computational neuroscience. Attitude toward experimental work and data analysis. Attitude for problem solving. Interests in understanding/learning basic biology.

References:

1. Mossink, B. *et al.* Human neuronal networks on micro-electrode arrays are a highly robust tool to study disease-specific genotype-phenotype correlations *in vitro.* Stem Cell Reports (2021).

2. Muzzi et al., Human-derived cortical neurospheroids coupled to passive, high-density and 3D MEAs: a valid platform for functional tests, Bioengineering (2023).

3. Doorn, N. *et al.* Breaking the burst: Unveiling mechanisms behind fragmented network bursts in patient-derived neurons, Stem Cell Reports (2024).

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