PhD Program in Bioengineering and Robotics

Curriculum Bioengineering and Bioelectronics

Research themes

The PhD Program for the Bioengineering and Bioelectronics curriculum provides interdisciplinary training at the interface between technology and biomedicine. The general objective of the program is to form research technologists capable to deal with multidisciplinary projects and to face complex challenges at the interface between technology and life-sciences. The training to the students is delivered through the in-depth involvement into a three-year research project supplemented by specific didactic modules dealing with computational and experimental methods. The direct link with different laboratories at both the Department of Informatics,

Bioengineering, Robotics and System Engineering (DIBRIS) and the Italian Institute of Technologies (IIT) 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:

- Biomedical imaging and medical information systems
- Bioelectronics, biomedical devices and bio-sensors
- Molecular, cellular and tissueengineering
- Neuroengineering and neurotechnology
- Micro and nano-systems in medicine and biology

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 (University Department or Italian Institute of Technology – IIT) where the research activity will be developed.
International applications are encouraged and will receive logistic support with visa issues, relocation, etc.

1. Neural computation in biological neuronal networks

Tutor: Sergio Martinoia

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

Description: We are interested in investigating how computational properties emerge in neuronal populations and how information processing and transmission is related to the topological properties of neuronal networks. The nature of representation depend on the structure of the neuronal networks in terms of connectivity, size and topology, and it is further constrained by the segmentation of activity to 'soft compartments' that are activated sequentially as well as in parallel, with mutual feedback among each other. In this project we propose to develop a systematic and controlled experimental and theoretical approach to focus on a specific question strictly related to the issue of neural computation: the interplay between structure and dynamics. For this aim, we will make use of in-vitro models constituted by patterned neuronal networks coupled to innovative high-density devices and advanced analysis tools to characterize and interpret the experimental data. This approach will be also complemented by artificially interfacing actual neuronal networks by means of microtrasnducer arrays capable of recording and stimulating the neuronal assemblies.

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

Reference: Kanagasabapathi T., Massobrio P., Barone RA., Tedesco M., Martinoia S., Wadman WJ., and Decré MJM, Functional connectivity and dynamics of cortical-thalamic networks co-cultured in a dual-compartment device, *J. Neural Eng.*, 9, 3, doi: 10.1088/1741-2560/9/3/036010 (2012).

Contacts: sergio.martinoia@unige.it

2. Development of synthetic models of neuronal assemblies

Tutors: Paolo Massobrio, Sergio Martinoia

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

Description: Behaviors require interaction with the environment and the contribution of different brain areas depending on the orchestrated activation of large neuronal assemblies. The present project aims at investigating by means of a computational approach, how to effectively interact with neuronal systems by understating the role of the network connectivity in the computational properties of small/large/interacting neuronal networks.
In particular, during the three-year research project, different computational network models will be developed and investigated, in order to:

i) characterize the spontaneous activity of networks of neurons with different connectivity rules, sizes, synaptic plasticity mechanisms. The observed dynamics will be investigated by checking whether particular configurations may promote phenomena like synchronization, emergence of critical phenomena, etc.
ii) characterize the stimulus-evoked activity induced by electrical stimulation in networks of neurons with different architectures. It will be investigated whether the evoked responses (i.e., the I/O function) can be modulated by structural connectivity.

Starting point for the development of these computational models and their parameters tuning are the recordings of both spontaneous and stimulus-evoked activity from cortical assemblies coupled to Micro-Electrode Arrays (MEas).

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

Reference: R. Russo, H.J. Herrmann, L. de Arcangelis. Brain modularity controls the critical behavior of spontaneous activity, *Scientific Reports*, vol. 4, doi: 10.1038/srep04312, 2014.

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3. Representing peripersonal space through sensorimotor likelihoods

Tutors: Silvio P. Sabatini, Fabio Solari

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

Description: While there is a growing evidence that the space immediately around the body (i.e., the *peripersonal space*) is coded in a distributed way across several coexisting reference frames, our knowledge of how different representations are aligned, adapt, and interact is still in its infancy. Where, when, and how does the brain implement the internal models underlying the sensorimotor transformations that guide both our actions and perceptions? Is the encoding of sensory information static, or does it change dynamically as the action unfolds? Looking for answers to these questions should help understanding how an agent should use sensing and proprioception-like signals dynamically to build sensorimotor representations of peripersonal space and self-calibrate.
Within the research framework developed in the PSPC lab at DIBRIS (see www.eyeshots.it), the activity will focus on the design of theoretical models by converting computational approaches from engineering into cortical-like models of implicit representations of the peripersonal space. Such implicit representations, besides advancing experimental predictions about neuronal activity, are expected to drive learning of meaningful interactions with the environment thus achieving fluid

multi-dimensional motor control in the presence of multiple sensory channels, and with minimal *a priori* knowledge.

Requirements: background in bioengineering, computer science, physics or related disciplines, strong interest in computational neuroscience.

Reference: Antonelli M., Gibaldi A., Beuth F., Duran A.J., Canessa A., Chessa M., Solari F., del Pobil A.P., Hamker F., Chinellato E. and Sabatini S.P. (in press) *A hierarchical system for a distributed representation of the peripersonal space of a humanoid robot*. IEEE Trans. on Autonomous Mental Development.

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4. Learning compositional visual representation of 3D shapes in vergent geometry

Tutors: Fabio Solari, Silvio P. Sabatini

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

Description (MAX 1500 char): It is plausible that the visual system develops convenient visual descriptors of 3D shapes concurrently with the capability of making binocular exploratory saccades on the surface of the observed objects. The joint treatment of the binocular vergence and of 3D perception still represents a challenging cognitive problem. Indeed, the zero-disparity condition in the fixation point solves the vergence task, but affects the visually-based depth information of the fixated object. Moreover, also *how* the system verge has an impact for the accuracy of stereopsis. Different eye positions can influence the local shape of the zero disparity surface near the fixation point (i.e., the surface horopter) and thus the mechanisms of perceptual vision.
The goal of proposed research is to derive a deep architecture for abstracting the statistically relevant information present in the disparity patterns obtained by the binocular fixations of an active stereo head. Starting from a neuromorphic early representation of 2D binocular disparity, the resulting 3D visual descriptors should be characterized by generalized perceptual constancy. The research will be conducted in collaboration with the Visual Cognitive System Lab of prof. Aleš Leonardis of the University of Ljubljana.

Requirements: background in bioengineering, computer science, physics or related disciplines, strong interest in computational neuroscience.

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5. Non-invasive methods for elevated intracranial pressure assessment

Tutors: Maura Casadio, Marek Czosnyka

Department: DIBRIS, University of Genoa
http://www.dibris.unige.it

Department of Neuroscience and Neurosurgery, University of Cambridge
Addenbrooke's Hospital, Hills Road CB22QQ Cambridge
http://www.neurosur.cam.ac.uk/

Description: Elevated intracranial pressure (ICP) is an important cause of secondary brain injury and its measure is often crucial for neurosurgical and neurological subjects. In most of acute neurological pathologies ICP is elevated and needs to be actively managed. This cannot be done without direct measurement, which is invasive and increases risk of infection and bleeding.
Non-invasive monitoring ICP is still a poorly-developed technique. It is clinically useful not only in developing countries to help victims of sub-tropical encephalophaties (including cerebral malaria), but also to monitor astronauts during long term space flights.
The research project is focused on comparison and refining methods for non-invasive ICP assessment based on transcranial Doppler ultrasonography and on the measurement of optic nerve sheath diameter.
It includes elements of mathematical modelling of cerebrospinal haemodynamics and CSF circulation and subsequent identification of the models. Recordings harvested in various clinical scenarios (head injury, subarachnoid haemorrhage, stroke, hydrocephalus, idiopathic intracranial hypertension) will be used and results cross-validated with direct ICP monitoring.

Requirements: Knowledge of Neuroscience, Biomedical Engineering, Physiology, Neuroanatomy, Neurointensive Care, Neurophysiology, Intracranial Pressure multimonitoring. Work experience in clinical settings.

Reference: Kristiansson H., Nissborg E et al. Measuring Elevated Intracranial Pressure through non invasive methods: a Review of Literature. J Neurosurg Anesthesiol 2013; 25: 372-385

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6. Tele-care and Tele-medicine

Tutors: Danilo Pani, Luigi Raffo

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

Description: The activity will be part of the international AAL project HEREiAM - *An interoperable platform for self care, social networking and managing of daily activities at home* coordinated by University of Cagliari http://www.hereiamproject.org/
The aim of HEREiAM is to help older adults to stay longer and independent at home by providing an innovative user-friendly technology able to support them during daily life activities. Our solution can be conceived as an integrated, smart platform which will allow elders to have access to a set of services directly from their TV set at home. The TV is present in our homes since more than 50 years and it is now part of our daily life in particular for older people that already spend much time in watching dedicated programs. Everybody can use a remote control without being afraid of making a mistake in the performance of very basic interactive functions. Therefore, a TV-based platform is a good solution to overcome the older adults traditional digital divide to use ICT systems. The HEREiAM system is designed for a specific target group of self-sufficient elderly people who want to be independent as long as possible in the management of personal and social tasks. The services provided by HEREiAM will meet needs expressed by households, giving them a sense of security, belonging and well-being at home.
The proposed theme of research concerns the conception, study and development of electronic devices for tele-care and tele-medicine and the study and development of proper hw/sw platforms.

Requirements: background in electronic engineering and bioengineering. Attitude for problem solving. Interests in experimental work.

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7. Organic Bioelectronics

Tutors: Annalisa Bonfiglio

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

Description: Organic Field Effect Transistors (OFETs) and Organic ElectroChemical Transistors (OECTs) have gained in recent years a considerable interest in the scientific community because of their potential in several fields of application related to the detection of biological species and samples that need to be measured with high precision, fast, reliable and possibly low-cost methods.
Several examples of OFET- and OECT-related sensors and biosensors have been presented with a variety of working principles, as, for instance, Ion Sensitive OFETs (ISOFETs), Electrolyte-Gated OFETs (EGOFETs), OTFTs, OECTs.
In a transistor, the channel current is normally modulated by varying the voltage applied across the dielectric layer between gate and source (taken as the reference terminal), i.e. any charge variation on the gate side is able to induce, by capacitive coupling across the gate dielectric, a current variation in the channel. Thus, a transistor is in fact a charge sensor and any bio- or chemo-reaction which implies or induces a charge variation on the gate could be in principle detected with this device.
The proposed theme of research concerns the development of these devices and, in particular, the specialization of these structures towards the detection of physical variables (as for instance temperature and/or strain) by means of piezo- and piroelectric materials at the interface between the device sensitive area the surrounding environment. Applications in the field of robotics, wearable monitoring systems, multimodal sensing will be addressed.

Requirements: background in bioengineering, electronic engineering, physics or related disciplines. Attitude for problem solving. Interests in experimental work in the lab.
Reference: M. Demelas, S. Lai, A. Spanu, S. Martinoia, P. Cosseddu, M. Barbaro, A. Bonfiglio “Charge sensing by Organic Charge-Modulated Field Effect Transistors: application to the detection of bio-related effects”, Journal of Material Chemistry B, 2013, published online 16.05.13, DOI: 10.1039/C3TB20237B

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8. Telomerase activity detection by organic electronic biosensor

Tutors: Massimo Barbaro

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

Description: The activity will be part of project AMBROSIA – *Pl**a**tfor**m** for **b**io-elect**r**onic detecti**o**n of expres**s**ion of telomer**a**se*.
AMBROSIA aims at developing a technology for rapid and real-time assessment of telomerase activity by the electronic measure of telomeres elongation.
Telomeres are the structures that protect chromosome ends from both recombination and degradation; they progressively shorten in replicating cells, thus their length represents a "biological clock" that determines cell senescence. Telomerase is able to avoid telomere shortening by synthesizing the addition of further hexanucleotide repeats in telomeric DNA. Elevated expression of telomerase is a key hallmark of human cancer and an indication of malignancy, while its reduced activity has been demonstrated in neurodegenerative diseases. Inhibition of telomerase is one of the most promising strategies for blocking the replication of cancer cells, while its re-activation has been shown to address amyotrophic lateral sclerosis. Telomerase is selectively expressed in very low natural abundance and the assays currently used have problems of speed, accuracy and reproducibility. AMBROSIA proposes overcoming these problems by developing reliable electronic systems based on the integration of biodevices realized in different technologies (CMOS, organic), microfluidic flow cells and appropriate surface chemistry.
The proposed theme of research concerns the conception, study and development of the electronic organic biosensor.

Requirements: background in electronic engineering and bioengineering. Attitude for problem solving. Interests in experimental work. Expertise in organic devices realization and DNA electronic detection.

Reference: Lai S., Demelas M., Casula G., Cosseddu P., Barbaro M., Bonfiglio A., "Ultralow voltage, OTFT-based sensor for label-free DNA detection", (2013) Advanced Materials, 25 (1), pp. 103-107.

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9. Biomechanical changes in cancer pathogenesis: integration of mechanical and genetics aspects to increase diagnosis accuracy

Tutors: Marco Fato, Silvia Scaglione, Massimo Vassalli

Department: DIBRIS, University of Genoa
http://www.dibris.unige.it

Description: Malignant transformation, though primarily driven by genetic mutations in cells, is also accompanied by specific changes in cellular and extra-cellular mechanical properties such as stiffness and adhesion. It has been highlighted, for example, that cell stiffness decreases in cells with higher malignancy and metastatic potential, that tumours with high invasive potentials have a stiffer extra-cellular environment, and that cancerous cells present increased acto-myosin cortex contractility as compared to corresponding healthy cells, thus significantly changing cytoskeleton properties. The potential of cancer biomechanics for the design of innovative diagnosis tools has been recently argued, but still we lack of a comprehensive understanding on how cells and tissues mechanical properties are correlated to, or influence, malignancy and staging of cancers.
This project aims at investigating the mechanical aspects exploiting advanced nanomechanical tools to perform high resolution mapping of mechanical properties in tissues and cellular populations. The onset of a clear biomechanical feature will be correlated with the genetic pattern of the biological system and the effect of environmental stimuli on living systems will be analysed. The overall activity will be carried out in close collaboration with domain experts, focusing on cancers of special interest and performing biological and functional validations on tissues obtained from biobanks.

Requirements: Background in biophysics, bioengineering, biotechnology or related disciplines.

Reference: M Plodinec, M Loparic, CA. Monnier et al. *The nanomechanical signature of breast cancer,* Nature Nanotechnology 7, 757–765 (2012)

Contacts: marco.fato@unige.it

10. Development of novel techniques for investigating stretch activated signaling in dystrophic skeletal muscle fibres

Tutors: Roberto Raiteri

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

Description: Duchenne Muscular Dystrophy (DMD), the most common muscular dystrophy, is a devastating, fatal, X-linked degenerative muscle disease that affects approximately 1 in 3500 male births. While it is unequivocal that the absence of dystrophin is the molecular cause of the disease, the latency of disease presentation

in humans and the murine model suggests that dystrophin deficiency alone does not explain the downstream muscle weakness and wasting. In DMD skeletal muscle, a growing body of evidence supports a model in which mechanical stress activates excessive calcium (Ca2+) influx and reactive oxygen species (ROS) production, two pathways critical for muscle damage and degeneration. Mechanisms for the mechano-transduction dependent activation of ROS and Ca2+ signaling are therefore crucial to understand the initiation and progression of the dystrophic phenotype.
In collaboration with the research group of Dr Christopher Ward at the University of Maryland, we recently discovered that in both heart and skeletal muscle fibres, the microtubule (MT) network is a critical element for the stretch activation of ROS: we demonstrated an age dependent increase in near membrane cytoskeletal stiffness in mdx as measured by Atomic Force Microscopy (AFM) that correlated with the augmentation of ROS and we also showed that the ROS and subsequent Ca2+ influx could be normalized by pharmacologically disrupting the MT network.
The aim of the proposed project is to develop novel tools by coupling atomic force microscopy, electro-actuated elastomer films, and fluorescence microscopy to directly assay mechano-signaling in single skeletal myofibers. With this approach we want to get novel mechanistic insights into the role of the dense MT network in DMD muscle and identify new cellular therapeutic targets to halt or slow the disease progression.

Requirements: background in bioengineering, biophysics or related disciplines. Attitude for experimental work and problem solving. Interests in understanding/learning muscle physiology.

Reference: Khairallah RJ *et al.* "Microtubules underlie dysfunction in duchenne muscular dystrophy" *Science Signaling*, 5(236):ra56. (2012)

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11. Development of an acoustic stimulation technology of genetically modified cells

Tutors: Michael Pusch, Roberto Raiteri

Department: Istituto di Biofisica (CNR) (www.ibf.cnr.it) and DIBRIS (University of Genova) http://www.dibris.unige.it

Description: The project aims at developing a novel strategy capable to modulate remotely and non-invasively the electrical activity of genetically modified heart and nervous cells *in vitro*, by using acoustic waves. Neurons and or cardiac myofibres will be genetically modified to over-express the recently identified mechanically activated *Piezo* ion channels. The sensitivity of these cells to direct contact stimulation and to remote acoustic stimulation shall be characterized in terms of the electrical and mechanical response as well as intracellular Ca^{2+} dynamics using

micro- and nano-electrode recordings, Ca^{2+} imaging and atomic force microscopy. The necessary technology to perform direct and remote acoustic stimulation combined with electrical/mechanical and Ca^{2+} dynamic readout will be developed and used to obtain a biophysical characterization of the mechano-response of the genetically modified cells (initially in simpler cell lines) at the molecular, cellular, and network level in order to prove the concept, get a better understanding of the Piezo channels working properties, and find optimal stimulation parameters for low-intensity, selective, and non-invasive stimulation. This technology could lead in the long term to the development of a novel class of neuroprosthetic cardiac stimulation devices.

Requirements: The ideal candidate holds a Master degree in experimental bioengineering/biophysics, has some knowledge in electrophysiology and possibly in cell and molecular biology, and is interested in the development of new experimental set-ups.

Reference: Coste B, Mathur J, Schmidt M, Earley TJ, Ranade S, Petrus MJ, Dubin AE, Patapoutian A. 'Piezo1 and Piezo2 are essential components of distinct mechanically activated cation channels', Science, 2010, 330:55-60

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12. ICT for data reuse in chronic infective diseases

Tutors: Mauro Giacomini

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

Description: DIBRIS, with infectious disease and immunology physicians, has developed the "Ligurian HIV Clinical Network", a web tool to manage clinical data from HIV1+ patients for clinical follow-up and multicenter clinical trials [1].
At present 2372 patient from 9 hospitals are involved, with 36283 laboratory exams results recorded. Possible development are:

- Expansion to other chronic viral diseases such as HCV and HBV
- Fully automate data entry
- Automatic data exchange with national and international multicenter clinical trials
- Ability to use data for "on demand" clinical research, based on European guide lines (ECRIN)
- Ability to monitor resistant bacterial infection

Using of standardized tools is required: clinical research main standard is Operational Data Model, while Healthcare Services Specification Program is the one for clinical care. In particular the Retrieve, Locate, Update Service Functional Model

will be used to manage clinical data through HL7 Clinical Document Architecture, while Common Terminology Services - Release 2 will administrate the definition of semantics and syntax.
This project takes into consideration aspects interesting for: European research, Italian national health system, regional health policy.

Requirements: direct reuse of clinical data, elements of standardization of medical information, tools for modeling web services, tools for the design and implementation of standardized services choreography according to the scheme HSSP.

Reference: P. Fraccaro, C. Dentone, D. Fenoglio, M. Giacomini "Multicentre Clinical Trials' data management: A hybrid solution to exploit the strengths of Electronic Data Capture and Electronic Health Records systems" Informatics for Health and Social Care, 2013; 38(4): pp. 313–329

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13. Towards a lab-on-a-chip super microscope by combining light and fluids

Tutors: Martí Duocastella, Alberto Diaspro

Department: Nanophysics (IIT)
http://www.iit.it/en/research/departments/nanophysics.html

Description: Scaling down a laboratory to fit on the palm of your hand (lab-on-a-chip or LOC) has many benefits. The sample and reagent volumes are reduced, the analysis speed is increased, integration and portability are achieved, and the unique behavior of fluids at the microscale allow a better process control. Fabricating such systems is extremely challenging, and methods have yet to be develop that produce the integration of sensors, microchannels and micromechanical actuators required in LOC. A promising approach to advance towards LOC consists in combining light and fluids (optofluidics). Notably, the unique properties of light enable one to manipulate objects in a non-contact way and to deliver energy at desired locations, which opens the door to efficient microfabrication, fluid actuation or enhanced sensing. In this PhD project, the candidate will work on the fabrication of microfluidic devices and on the integration of optical detection systems in LOC. This is a multidisciplinary project that covers aspects of material science, optics and fluids. It is part of a long term program for realizing lab-on-a-chip multimodal microscopes, including super resolution approaches.

Requirements: background in engineering and bioengineering, physics and biophysics, material science, or chemistry. We are looking for a highly motivated candidate with strong experimental attitude along with a permanent interest in learning new things.

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14. Investigation of biological organization at the nanoscale with advanced optical microscopy methods: application to chromatin

Tutors: Luca Lanzano, Alberto Diaspro

Department: Nanophysics (IIT)
http://www.iit.it/en/research/departments/nanophysics.html

Description: Even though the composition and structure of many biological macromolecules has been established, little is known about the complex organization at the level between 10nm-100nm, mostly because this region has not been accessible by conventional optical microscopy. Understanding how nuclear chromatin folds into higher order structure[1] is still an open challenge in spite of its strong potential impact in biology, medicine and bioengineering, for example towards pre-neoplastic diagnosis, monitoring of drug effects or new engineering approaches in biomimicry. Advanced optical microscopy methods pushed to the nanoscale represent a unique opportunity to investigate this process with minimal perturbation. These methods include for instance fluorescence-based super-resolution techniques (e.g. Stimulated Emission Depletion microscopy), dynamic single molecule approaches (Fluorescence Correlation Spectroscopy, Single Particle Tracking), CIDS (Circular Intensity Differential Scattering) imaging or a combination of them [2]. These methods will be optimized for live cell observations in combination with labeling methods which preserve native chromosome structure.
Requirements: This is an interdisciplinary theme. Background in engineering/bioengineering, biophysics, applied physics or related disciplines (with interest in understanding/learning basic biology) or background in biology or related disciplines (with interest in advanced biophysical methods).

Reference: Q. Bian and A.S. Belmont, Revisiting higher-order and large-scale chromatin organization. *Current Opinion in Cell Biology* (2012) 24:359–366; [2] A.Diaspro, Nanonoscopy and Multidimensional Optical Microscopy (2010) Chapman/CRC.

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15. Nanocrystal as probe for super-resolution microscopy

Tutors: Giuseppe Vicidomini, Alberto Diaspro

Department: Nanophysics (Italian Institute of Technology)
http://www.iit.it

Until not very long ago, it was widely accepted that diffraction limits the spatial resolution of a light microscope to about half of the wavelength of light. In the 90's

and 2000's, the advent of viable physical concepts for circumventing the diffraction limit set off a quest that has led to readily applicable and widely accessible fluorescence microscopes with nanoscale spatial resolution, usually referred as super-resolution microscopes. A class of these super-resolution microscopes is based on spatially non-uniform illumination of the sample and nonlinear photoresponse of the probe as function of the illumination intensity [1].
Colloidal nanocrystals (NCs) have proven to be a versatile class of nanomaterials with potential applications in bio-labels. They are characterized by excellent photo-stability and high quantum-yield, which are key requisites for fast and long-term imaging.
This project, in collaboration with Iwan Moreels of the IIT-NACH and Colin JR Sheppard of the IIT-NAPH, aims to investigate the non-linear photo-response of NCs as a suitable mechanism at the basis of new super-resolution microscopy techniques. Also non-linear photorespone induced by stimulate emission (typical of stimulated-emission-depletion microscopy) will be considered. Engineering of such an approach towards biological applications in vivo is an important challenge in modern bioimaging.

Requirements: The candidates should have a background in engineering/bioengineering, bioelectronics, physics/biophysics or related disciplines. Enthusiasm, an interdisciplinary attitude, and a strong team spirit in an interdisciplinary environment are a must.

Reference:

Heintzmann, R. and Gustafsson, M. G. L. Subdiffraction resolution in continuous samples. *Nature Photonics*, 3:362-364 (2009)

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16. Confocal microscopy with detector array

Tutors: Giuseppe Vicidomini, Alberto Diaspro

Department: Nanophysics (Italian Institute of Technology)
http://www.iit.it

Fluorescence microscopy in general, and confocal microscopy in particular, is an essential tool in life science, as well as in materials science. In a confocal microscope, the objective lens focuses a laser beam on a specific sample position; the emitted fluorescence is collected by the same objective, passes through a pinhole and is measured by a single point detector. Finally, scanning the beam across the sample reconstruct the sample morphologies (imaging) or/and analyzing the fluorescence fluctuations along the time reveals the sample dynamics (fluorescence-correlation-spectroscopy (FCS))
This project, in collaboration with Francesca Cella Zanacchi and Colin JR Sheppard of the IIT-NAPH, aims to develop the next generation of confocal microscopy. Since a

single point detector averages the signal along its sensitive area and along the probing time, many spatial and time information are canceled out. The successful candidate will substitute the point detector and the pinhole with an array of fast detectors. This solution could improve the spatial resolution of the imaging system, as recently demonstrated with similar "pixel-reassignment" architecture [1], and serve as platform for dynamic investigation at high temporal and spatial resolution. In particular, the very same system can be used to perform single molecule tracking inside the diffraction-limited area probed by the focused laser beam. Further, the possibility to monitor the fluorescence signal over different neighbored detector allows implementing method of tracking with active feedback.

Requirements: The candidates should have a background in engineering/bioengineering, bioelectronics, physics or related disciplines and experience in programming. Enthusiasm, an interdisciplinary attitude, and a strong team spirit in an interdisciplinary environment are a must.

Reference: C. Sheppard, S. Mehta, and R. Heintzmann, Superresolution by image scanning microscopy using pixel reassignment, *Opt. Lett*. 38:2889-2892 (2013).

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17. Community detection in biomolecular networks

Tutors: Francesco Masulli, Stefano Rovetta

Department: DIBRIS (University of Genova)
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Description: Inferring groups of interacting proteins or genes with biological significance is a main trend of the current bioinformatics research, as this task can help in revealing the functionality and the relevance of specific macromolecular assemblies or even in discovering possible macromolecules affecting a specific biological process. Protein and gene interaction networks can be modeled similarly to social interaction networks, so that these biologically significant groups correspond to communities. Reliable algorithms able to discover such communities may increase knowledge about biological functions at a molecular level, and may support drug discovery and enhance disease treatments even in earlier stages. This project is aimed at the development of effective tools for community detection in biological networks using methods of network and graph theories, machine learning, and computational intelligence. For instance, a significant application goal, important for cancer biomarker research, is a better understanding of the role of miRNAs, a novel class of non-coding RNA able to modulate the expression of their "target" genes. The available algorithms, mostly based on structural information, are still not able to provide a biological enrichment of their results, that can instead be obtained from the proposed analysis.

Requirements: background in computer science, bioengineering, computer engineering, physics or related disciplines.

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