Bio-Nano Electronics and BioMolecular Computing

Course topic

Techniques and technologies for the detection and the use of biomolecules for nanoelectronics, in the domains of biomolecular sensing, diagnostics (DNA, proteins), biomolecular devices and bio-nanocomputing.

Number of credits
5 ECTS

Course responsible
Politecnico di Torino
Department of Electronics and Telecommunications
Prof. Danilo Demarchi

Course lecturers
Prof. Sandro Carrara (EPFL Lausanne, Switzerland)
Prof. Danilo Demarchi (Politecnico di Torino, Italy)
Prof. Yuval Garini (Bar Ilan University, Israel)
Prof. Yosi Shacham (Tel Aviv University, Israel)

Prerequisites
Knowledge of basic microelectronic technologies and of electronic devices. Basic principles of organic chemistry and sensing techniques.

Learning outcomes

Knowledge: basics of quantum mechanics useful for the modelling, design and use of bio-nanodevices, in particular bio-nanosensors. Knowledge of device fabrication techniques of bio-nanosystems.

Skills: modelling of biomolecules. Design of nanosystems for sensing and computing, choosing the needed interfaces for reading the signals and transferring the information, from the nanolevel to the user interface.

Competences: the students will reach a sufficient knowledge and skill for being able of choosing novel solutions in terms of bio-nanodevices and bio-nanosensors, with the capability of guiding the strategical choices for the implementation of nanoelectronic devices and systems based on biomolecules.

Abstract

The course aims to introduce the use of biomolecules for the realization of innovative devices, sensors and computing systems.

Yuval Garini – DNA & proteins: Structure, properties, detection and characterization

We will start by summarizing the structure of DNA, RNA and proteins, its principle chemical, physical and biological properties and its main functions. This will provide the basis for understanding how the methods for detecting these important elements of life can be detected, or being used for detection.
Then, we will summarize fundamental methods for detecting DNA/RNA and proteins. These methods vary from chromatography on one hand through electrophoresis, all the way to imaging techniques that takes advantages of fluorescent stains and novel microscopy methods.
Finally, we will describe the use of DNA and proteins themselves as probes for measuring important biomedical parameters, as well as for treating diseases and even cancer.

Yosi Schacham - Nanomaterial based electrochemical biosensors

Then, different technologies for biosensing are analyzed. It is presented a review of electrochemical sensors in general and biological applications in particular. The main applications are in the fields of medicine and healthcare, food and agro and environment. Initially it is presented an overview of the fundamentals of applied electrochemistry for both nano fabrication and the application of nano scale electrochemical devices. A short review of the basic electrochemical theory are analyzed, followed by a review of basic electrical (DC &AC) and also optical characterization methods of such sensors. Next, a review of conventional microelectrodes is presented in general and the use of nano-material based electrodes in particular. Finally, few electrode systems are demonstrated; for example, 1. Silicon nano wire electrodes, 2. Metal (i.e. Au, Pt, AuPt etc.) nano particle on conjugate polymers electrodes and 3. Inkjet printed silver nano-particle electrodes modified by electroless plating. Enzyme based sensors using nano-structured electrodes tested by both amperometric and electrochemical impedance spectroscopy are described.

Sandro Cararra - BioMemristors

The course continues describing electrochemical biosensors based on a memristive effect and aptamers or antibodies. These novel sensing devices are developed to propose a completely new approach in the co-design of Bio/Nano/CMOS interfaces for cancer diagnostics. Affinity-based techniques are studied for the detection of the prostate specific antigen (PSA) and the Vascular Endothelial Growth Factor (VEGF). The hysteretic properties of memristive silicon nanowires functionalized with proper biomolecules provide a label-free and ultrasensitive bio-detection technique. In order to develop full systems for diagnostics, the integration with CMOS frontend, in one side of the interface, and microfluidics, in the other side, is required too. Therefore, are discussed novel circuit approaches for an automated and quick characterization of arrays of memristive biosensors. One memristive parameter, the width of the voltage gap, is directly proportional to the target molecules concentration. Thus, CMOS readouts acquiring such width, meanwhile sorting-out faulty devices, i.e. non- conducting nanowires in the array, are presented

together with analog-to-digital conversion for the acquired voltage gap. A prototype of these circuits is shown as an example of design in 0.35µm CMOS technology. The integration of the CMOS readout with the nanoscale sensors and a microfluidic platform is a must for the design of robust biosensing-systems for quick data acquisition in cancer diagnostics. Therefore, the development of an improved chip-platform for cancer diagnostics based on nanofabricated Memristive Biosensors integrated, for the first time, with a microfluidic structure is also presented in this lecture by also addressing critical issues, e.g., the problems related to long connections between the Memristive Biosensors and the CMOS frontend.

Danilo Demarchi - BioNanoComputing

The course ends with the introduction to the reasons why a change in computing paradigm is an actual opportunity exploiting biomolecules. Novel circuits and systems for computations that are expected to become the main actor in the forthcoming scenario are presented, going beyond the ultra-scaled CMOS technologies and focusing the attention on the emerging technologies.
Finally, detailed examples of bio-computing systems are described, using DNA as in the solution of NP-complete problems as the Hamiltonian path (or the Travelling Salesman Problem) done by the Adleman Experiment. Then computing solutions based on Enzymes, Antibodies/Antigens and Cells are described and analyzed.

Content

1. DNA, RNA and proteins
   1.1. The structure of DNA, RNA and proteins
   1.2. Chemical and physical properties of the biological structure
   1.3. Biological function of the structures
   1.4. Detection methods of the entities
   1.5. Using DNA and proteins as sensors
   1.6. Using DNA and proteins as nano structures for drug delivery

2. Nanomaterial based electrochemical biosensors
   2.1. Review of electrochemical sensors and related biological applications
   2.2. Fundamentals of applied electrochemistry
   2.3. Basic electrochemical theory
   2.4. Electrical (DC &AC) and Optical characterization methods
   2.5. Conventional microelectrodes
   2.6. Electrode systems
      2.6.1. Silicon nano wire electrodes
      2.6.2. Metal (i.e. Au, Pt, AuPt etc.) nano particle on conjugate polymers electrodes
      2.6.3. Inkjet printed silver nano-particle electrodes modified by electroless plating.
   2.7. Enzyme based sensors using nano-structured electrodes tested by both amperometric and electrochemical impedance spectroscopy are described.

3. BioMemristors
   3.1. Electrochemical biosensors based on memristive effect
   3.2. Affinity-based techniques

3.3. Hysteretic properties of memristive silicon nanowires
3.4. Novel circuit approaches for an automated and quick characterization of arrays of memristive biosensors
3.5. CMOS readouts and analog-to-digital conversion
3.6. Integration of CMOS readout with nanoscale sensors and microfluidics
3.7. An improved chip-platform for cancer diagnostics

4. Biomolecular NanoComputing
   4.1. Introduction to use of biomolecules for computing
   4.2. DNA and the Adleman Experiment
   4.3. Proteins, antingen and antibodies as computing bricks
   4.4. Cells as computational machines

Teaching methods

The course is presented in the Moodle learning environment in the form of videos and supporting material as PDF slides.

Assessment

The evaluation is based on a Scientific Report that the student will prepare, related to one of the topics presented inside the course.

Recommended readings

[1] Carrara S. (2011). *Nano-Bio-Sensing*, Springer Ed., 2014.
[2] Carrara S. and Iniewski K. *Handbook of Bioelectronics - Directly Interfacing Electronics and Biological Systems*, Cambridge University Press, 2015.
[3] Rigler, R., & Vogel, H. *Single Molecules and Nanotechnology,* Springer Ed., 2007.
[4] Katz, E., *Molecular and Supramolecular Information Processing*, Wiley-VCH, 2012 .
[5] Katz, E., *Biomolecular Information Processing*, Wiley-VCH, 2012.

LECTURERS' CURRICULA

Prof. Yuval Garini is a member of the Physics Department and the Nanotechnology Institute in Bar Ilan University since 2007. He is the head of the Bar Ilan Institute for Nanotechnology (BINA) since 2013. He is heading the Nano-Bio-Photonics laboratory that he established since 2007. He received his Ph.D. in Physics from the Technion Institute in Israel in 1994. Before that he was a member of the Applied Physics department in Delft University, the Netherlands. After his graduation, Prof. Garini established a company that developed advanced systems for biomedical applications and genetic analysis. Prof. Garini's research focuses on the exploration of biological systems by combining advanced optical, imaging and single molecule methods, nano-structures and biophysical modeling. He is studying fundamental question of living entities, such as the organization of the genome in the nucleus as well as other dynamic processes in live cells. He is

active in various national and international organizations including the Israel Physical Society, Israel Biophysical Society and the American Biophysical Society

Prof. Yosi Shacham–Diamand is a professor for electrical engineering at the department of electrical engineering, physical electronics, school of electrical engineering and also in the department of materials science and engineering, both at the faculty of engineering Tel Aviv University. He got his D.Sc. EE 1983, M.Sc. EE 1978, and B.Sc. EE (Summa-cum Laude) 1974, all in Technion, Israel. 1983-1986 post-doctorate at U.C. Berkeley. 1987- 1989 senior lecturer, the Technion, Israel. 1989-1996 assistant professor Cornell university, 1997-2001 Associate professor and since 2001 a full professor at the school of electrical engineering, Physical Electronics department, Tel-Aviv University. He is a Visiting professor, CNR-IMM, Rome, Italy, Visiting Professor, Waseda University, Tokyo, Japan and a distinguished international chair professor, Feng Chia University.
He published >220 journal papers, >300 conference papers in registered proceedings, 4 chapters in books, 20 patents, edited two conference proceedings books, and two books. Currently he is a member of the Israeli National committee for generic technology (MAGNET), office of the chief scientists, ministry of economy.
He is a member of the advisory committee of the advanced metallization conference (AMC), the Materials for Microelectronic (MAM) conference and electrochemical micro and nano technologies (EMNT). He is a member of the editorial board of the Journal of Micro Electronics Engineering and the editor of special issues in the Journal of Micro Electronics Engineering and Electrochimica Acta.
His research activity is in the field of micro and nano fabrication and metallization science and technology. For more than 25 years he investigates electroless plating micro and nano fabrication for various applications such as for microelectronics, micromachining, and biochips. For the last 15 years, he conducts also a significant research program on whole cell biochips and solid-state biosensors.

Prof. Sandro Carrara is an IEEE Fellow for his outstanding record of accomplishments in the field of design of nanoscale biological CMOS sensors. He is also the recipient of the IEEE Sensors Council Technical Achievement Award in 2016 for his leadership in the emerging area of co-design in Bio/Nano/CMOS interfaces. He is a faculty member (MER) at the EPFL in Lausanne (Switzerland). He holds a PhD in Biochemistry & Biophysics from University of Padua (Italy), a Master degree in Physics from University of Genoa (Italy), and a diploma in Electronics from National Institute of Technology in Albenga (Italy). His scientific interests are on electrical phenomena of nano-bio-structured films, and include CMOS design of biochips based on proteins and DNA. Along his carrier, he published 7 books, one as author with Springer on Bio/CMOS interfaces and, more recently, a Handbook of Bioelectronics with Cambridge University Press. He also published more than 200 scientific papers and is author of 12 patents. He is Associate Editor-in-Chief of the IEEE Sensors Journal; he is also founder and Editor-in-Chief of the journal BioNanoScience by Springer, and Associate Editor of IEEE Transactions on Biomedical Circuits and Systems. He is a member of the Board of Governors (BoG) of the IEEE Circuits And Systems Society (CASS). He is member at large of the IEEE Sensors Council. He has been appointed as IEEE CASS Distinguished Lecturer for the years 2013-2014. His work received several international recognitions: several Top-25 Hottest-Articles (2004, 2005, 2008, 2009, and two times in 2012) published in highly ranked international journals such as Biosensors and Bioelectronics,

Sensors and Actuators B, IEEE Sensors journal, and Thin Solid Films; a NATO Advanced Research Award in 1996 for the original contribution to the physics of single-electron conductivity in nano-particles; three Best Paper Awards at the IEEE PRIME Conference in 2015 (Glasgow), in 2010 (Berlin), and in 2009 (Cork), a Best Poster Award at the Nanotera workshop in 2011 (Bern), and a Best Poster Award at the NanoEurope Symposium in 2009 (Rapperswil). He also received the Best Referees Award from the journal Biosensor and Bioelectronics in 2006. From 1997 to 2000, he was a member of an international committee at the ELETTRA Synchrotron in Trieste. From 2000 to 2003, he was scientific leader of a National Research Program (PNR) in the field of Nanobiotechnology. He was an internationally esteemed expert of the evaluation panel of the Academy of Finland in a research program for the years 2010-2013. He has been the General Chairman of the Conference IEEE BioCAS 2014, the premier worldwide international conference in the area of circuits and systems for biomedical applications.

Prof. Danilo Demarchi is Associate Professor at Politecnico di Torino, Department of Electronics and Telecommunications, with the tenures of “Bio-Micro&Nano Systems” for Biomedical and Electronics Engineering, of “CAD for Microsystems” for Electronics Engineering and Nanotechnologies for ICT, and of “NanoElectronics” for the PhD School in Electronics and Telecommunications. He is teaching too some training modules in the course of “Micro&Nano Systems” for Electronics Engineering and Nanotechnologies for ICT, and the courses of “Molecular Electronics” and “Nanocomputing” for the PhD School in Electronics and Telecommunications.
He is Lecturer at EPFL Lausanne for the course "Nanocomputing", Biomolecular computing module, at the Electrical Engineering PhD School and Associate Faculty at the University of Illinois at Chicago, Department of Electrical and Computer Engineering.
Currently working on micro and nano systems for electronics and biomedical applications. Author and co-author of 3 patents and of about 200 scientific publications in journals and peer-reviewed conference proceedings.
Currently he is leading the MiNES (Micro&Nano Electronic Systems) Laboratory of the Politecnico di Torino. He was and is Coordinator or Partner of many European Projects in FP6, FP7 and Horizon2020.
Member of many Scientific Journal and Conference Committees, the most recent ones are: nominated General Chair of IEEE BioCAS 2017, Torino, Italy; Tutorials and Keynotes Co-Chair, IEEE BioCAS 2016, Shanghai, China; Technical Program Chair of Special Session on Design of Cyber-Physical Systems, DSD2016, Nicosia, Cyprus; Associate Editor, Section Bioinstrumentation, Biosensors and Bio-Micro/Nano Technologies, Annual IEEE EMBC (Engineering in Medicine and Biology) Conference, Milan, Italy; Co-Chair of CMOS Lab-on-Chip Track, IEEE ISCAS 2015, Lisbon, Portugal; Track Co-Chair, Analog circuits and systems, IEEE NewCAS 2015, International NEW Circuits and Systems Conference, Grenoble, France; Scientific Committee, IEEE IWASI 2015, International Workshop on Advances in Sensors and Interfaces, Bari, Italy; Special Session Chair Member, Bio-Inspired Circuits and Systems for Robotics, IEEE BioCAS 2014, Lausanne, Switzerland.
He is Senior Member of IEEE, Member of the BioCAS Technical Committee and Member of the Steering Committee of BioCAS Conference, Member of AENEAS (Association for European NanoElectronics ActivitieS) Scientific Council, Member of the “Outside System Connectivity” working group, European Nanoelectronics Infrastructure for Innovation Consortium.

Associate Editor of IEEE Transactions on Biomedical Circuits and Systems, of IEEE Sensors and of the Springer Journal BioNanoScience.

Memristor Technology for Cognitive Computing

Course topic

Techniques and technologies for the design of memristor-based nonlinear circuits as fundamental building-block of advanced cognitive intelligent systems.

Number of credits
3 ECTS

Course responsible
Prof. Fernando Corinto
Politecnico di Torino, Department of Electronics and Telecommunications

Course lecturers
Prof. Fernando Corinto (Politecnico di Torino, Italy)

Prerequisites
Knowledge of basic circuit theory and of electronic devices. Basic principles of nonlinear dynamics.

Learning outcomes

Knowledge: basics of physics for circuit modeling, analysis and design, in particular nonlinear circuit theory. Knowledge of nonlinear differential ordinary equations and nonlinear analysis.

Skills: modelling of nanoelectronic devices and circuit analysis. Qualitative analysis on nonlinear dynamical systems (equilibrium points, periodic/chaotic attractors and bifurcation phenomena).

Competences: students will reach a sufficient knowledge and skill for being able to analyze and design nonlinear circuits with memristors. In addition, students will acquire the fundamental principles of neural networks and machine learning algorithms.

Abstract
After the computer and internet revolutions in the last 50 years, internet of things (IoT) promises to be the next big technology revolution deeply impacting all aspects of human life, e.g., industrial processes, health, transport, communication, and many others. The retrieve of relevant information from massive amount of data will soon be impossible with conventional computers due to physical limitations.
A major challenge is to bring sufficient intelligence on board of the system, while maintaining reasonably low power consumption and real time reconfiguration. Such objective might be achieved via memristive hardware, which has recently raised increasing interest as low power, high density systems for learning and recognition of patterns, such as handwritten characters,

faces, and speech. In this course I will present work that has been done towards the development of memristor-based cognitive systems. In particular the talk covers the fundamental theory of memristor circuits and their nonlinear dynamical properties (e.g. synchronization, spatio-temporal pattern, ...), the spiking computing principles with memristor synapses and the use of memristor networks in pattern recognition tasks.

Content

- Overview of existing memristor technology
  - Background and Challenges
  - Organic and Inorganic Memristor Devices
- Memristor Circuits
  - Fundamental Theory of Memristor
    - Flux-Charge Analysis Method
    - Nonlinear Dynamics in Memristor Circuits
  - Memristor Oscillators
    - Synchronization and Oscillatory Associative Memories
  - Memristor Arrays
- Cognitive computing,
  - Bioinspired memristor circuits: 1T1R and 2T1R synapses
  - Neuromorphic Computer Architectures

Cellular Nanoscale/Nonlinear Networks with Memristors

Teaching methods

The course is presented in the Moodle learning environment in the form of videos and supporting material as PDF slides.

Assessment

The evaluation is based on a Scientific Report that the student will prepare, related to one of the topics presented inside the course.

Recommended readings

[1] F. Corinto, A. Ascoli, and M. Gilli, "Nonlinear dynamics of memristor oscillators," IEEE Trans. Circuits Syst. I, vol. 58, no. 6, pp. 1323–1336, 2011.

[2] Kozma, Robert, Robinson E. Pino, and Giovanni E. Pazienza, eds. *Advances in neuromorphic memristor science and applications*. Vol. 4. Springer Science & Business Media, 2012.

[3] Tetzlaff, Ronald, ed. *Memristors and memristive systems*. Springer Science & Business Media, 2013.

[4] Adamatzky, Andrew, and Leon Chua, eds. *Memristor networks*. Springer Science & Business Media, 2013.

[5] F. Corinto, P. P. Civalleri, and L. O. Chua, "A theoretical approach to memristor devices," Emerging and Selected Topics in Circuits and Systems, IEEE Journal on, vol. 5, no. 2, pp. 123–132, 2015.

[6] F. Corinto and M. Forti, “Memristor circuits: Flux–charge analysis method,” IEEE Trans. Circuits Syst. I, Reg. Papers, vol. 63, no. 11, pp. 1997–2009, November 2016, DOI: 10.1109/TCSI.2016.2590948.
[7]
[8] F. Corinto and M. Forti, “Memristor circuits: Bifurcations without parameters,” IEEE Trans. Circuits Syst. I, Reg. Papers, vol. 64, 2017, published online. DOI: 10.1109/TCSI.2016.2642112.
[9] Suri, Manan. *Advances in Neuromorphic Hardware Exploiting Emerging Nanoscale Devices*. Springer Science and Business Media, 2017.

LECTURER's CURRICULUM VITAE

Prof. Fernando Corinto received the Masters' Degree in Electronic Engineering and the Ph.D. degree in Electronics and Communications Engineering from the Politecnico di Torino, in 2001 and 2005 respectively. He also received the European Doctorate from the Politecnico di Torino, in 2005. Prof. Corinto was awarded a Marie Curie Fellowship in 2004.
He is currently Associate Professor of Circuit Theory with the Department of Electronics and Telecommunications, Politecnico di Torino. His research activities are mainly on nonlinear circuits and systems, locally coupled nonlinear/nanoscale networks and memristor nanotechnology.
Prof. Corinto is co-author of 6 book chapters and more than 120 international journal and conference papers. Since 2010, he is Senior Member of the IEEE. He is also Member of the IEEE CAS Technical Committees on “Cellular Nanoscale Networks and Array Computing” and “Nonlinear Circuits and Systems”. Prof. Corinto serves as Vice-Chair of the IEEE North Italy CAS Chapter. Prof. Corinto has been Associated Editor of the IEEE Trans. on Circuits and Systems - I for 2014-2015. He is also in the Editorial Board and Review Editor of the International Journal of Circuit Theory and Applications since January 2015. Prof. Corinto is Vice Chair of the COST Action “Memristors - Devices, Models, Circuits, Systems and Applications (MemoCiS)”. Prof. Corinto has been DRESDEN Senior Fellows at the Technische Universität Dresden in 2013. Prof. Corinto is also August-Wilhelm Scheer visiting professor at Technische Universität München and member of the Institute for Advanced Study -Technische Universität München.