PhD in Information Technology and Electrical Engineering

Università degli Studi di Napoli Federico II

PhD Student: Emilio Andreozzi

XXXIII Cycle

Training and Research Activities Report – First Year

Tutor: Prof. Mario Cesarelli – co-Tutor: Prof. Paolo Bifulco

Università degli Studi di Napoli Federico II

1. Information

I received a M. Sc. Degree, cum laude, in Electronic Engineering from University of Naples Federico II in July 12th 2017 with the thesis “Design and implementation of a device for contactless monitoring of pacemaker activity”. I belong to the XXXIII PhD cycle in Information Technology and Electrical Engineering (ITEE), and my fellowship is financed by European PON project funds. My tutors are Prof. Mario Cesarelli and Prof. Paolo Bifulco.

2. Study and Training activities

During my first year of PhD I followed courses to enrich my knowledge in Digital Electronics Design and in Green Economy Project Design. I also attended two PhD schools and several seminars in different topics of Information Technologies. Finally, I participated to the IEEExtreme Programming competition, organised by IEEE, joining the team of the IEEE Federico II - Napoli Student Branch.

a. Modules
- System-on-Chip – Prof. Nicola Petra [9 ECTS]
- Morphic Sensing – Dr. Gaetano Gargiulo [2.4 ECTS]
- IEEExtreme Programming competition – Prof. Paolo Maresca [3 ECTS]
- How to publish a scientific paper – Aliaksandr Birokou [0.4 ECTS]

b. Seminars
- PhD School “XXXVII Scuola Annuale di Bioingegneria. Immagini biomediche: nuove tendenze in tecnologia, metodi e applicazioni”. – Gruppo Nazionale di Bioingegneria [5 ECTS]
- “From medical imaging to surgical planning: new directions for Bone and Muscle Assessment.” – Prof. Paolo Gargiulo [0.4 ECTS]
- “Using electroencephalography (EEG) to investigate the role of neo-cortical brain in postural control and postural adaptation when exposed to vibratory proprioceptive stimulation” – Prof. Paolo Gargiulo [0.4 ECTS]
- “Tomografia a contrasto di fase” – Ing. Pasquale Memmolo [0.4 ECTS]
- “Network Analysis, Data Sciences and Control in Computational NeuroScience” – Prof. Panos Pardalos [0.2 ECTS]

c. External courses (modules)
- PhD School on “Reliability in Electronics” – Società Italiana di Elettronica [4 ECTS]
- Green Economy Management in Engineering Projects – Prof. Giuseppe Zollo, Prof. Luca Iandoli [3 ECTS]

	Credits year 1							
	Estimated	bimonth 1	bimonth 2	bimonth 3	bimonth 4	bimonth 5	bimonth 6	Summary
Modules	20	0	0	7	2,4	3	9,4	21,8
Seminars	5	0	0	0,8	0	5,4	0,2	6,4
Research	35	8	8	3	3	2,8	7	31,8
	60	8	8	11	5,4	11	17	60

3. Research activity

- Main research topic:

  Improvements of noise suppression for low-dose X-ray imaging – Video fluoroscopy is a medical imaging technology able to provide continuous real-time X-ray screening of patient's body parts (also highlighted by contrast agents), as well as various surgical instruments, catheters, wire-guides, and prosthetic implants. Thus, it is an invaluable tool for minimally invasive image-guided diagnosis and treatment of diseases (orthopaedic surgery, angioplasty, pacemaker and defibrillator implantation, investigations of gastrointestinal tract or blood vessels, assessments of joints and implanted prosthesis [1,2,3,4,5]). The potentially dangerous effects of such ionizing radiations impose to limit human exposure, i.e. to keep patient's dose sufficiently low. Unlike radiography, which requires very small exposure times and can employ a sufficiently high power of radiation, obtaining a good Signal-to-Noise Ratio (SNR), fluoroscopy may require very long and unpredictable exposure times and, so, power must be kept sufficiently low as to limit the patient's dose, thus obtaining very poor SNR. In fact, the limited number of X-ray photons per pixel gives rise to a signal-dependent, Poisson-distributed noise, also known as "quantum noise" [6], which causes a significant decrease in the SNR. Quantum noise is by far the most dominant noise source in low-dose X-ray images [7,8] and cannot be avoided by improving detectors technology, since it is inherent to the image formation process. Commercial fluoroscopic devices usually address this issue both by reducing the frame rate (which produces the same effect of a temporal average filtration) or by introducing simple spatial averaging filters, in order to preserve the real-time operation: this is fundamental for all those applications which require to promptly perform an action in response to what is happening within patient's body. However, both temporal and spatial averaging tend to produce undesirable blurring effects, which undermines the preservation of edges and produces motion blur.

  Cesarelli, Bifulco et al. proposed a denoising algorithm based on conditioned spatio-temporal average filter, which performs the average only on pixels belonging to noise statistic, i.e. pixels having a standard deviation less than or equal to a multiple of the standard deviation of noise [9]. This strategy significantly reduces the blurring effects caused by simple averaging filters, outperforming several state-of-the-art algorithms in the denoising of X-ray images [10], while keeping the computational burden low enough to allow real-time hardware implementation [11].

  My research activity was aimed at improving this approach, so, at the beginning I focused on the analysis of the literature regarding advanced denoising algorithms for images and videos affected by Poissonian and Gaussian noise, in order to understand state-of-the-art approaches and their limitations. Then I started an experimental activity to compare the performances of the approach proposed by Cesarelli, Bifulco et al. with state-of-the-art video denoising algorithms (VBM4D, among others), since [10] compared its performances only in terms of single images processing, not taking into account the issues related to the time domain (e.g. motion blur). Finally, I started an experimental activity for the development of a new denoising algorithm for Poisson noise, both in software, focusing on parameters optimization, and in hardware, working on the implementation of the algorithm on a Field Programmable Gate Array (FPGA) platform.

- Other research topics:

  Contactless device for pacemaker pulse detection – A pacemaker is an active implantable medical device generally used to treat bradyarrhythmias, which are pathologies related to the depression or absence of heart beats. Many pathologies treated by pacemaker evolve over time and the continuous adjustment of pacing parameters can improve the efficacy of treatment and offer more benefits to the patient [12,13,14]. However, documentation of patient arrhythmias remains limited by the unreliability of patient symptoms and the need to document the pathology using short- or long-term surface ECG recordings (a Holter device can provide only few days of monitoring with the need to wear electrodes) [15]. For this reason, many pacemakers incorporate some event recorders and counters [16]. As an example, statistics on the occurrence of pacing pulses can be used to measure the evolution of arrhythmias and eventually to tune the electrical or pharmacological therapy. However, not all pacemakers are equipped with event recorders and then provide only concise statistics about pacing, but not information about each pulse timing. So, all implanted patients must undergo periodic check-ups [17] in order to verify the correct operation of the pacemaker and eventually to reprogram it for optimal therapy as well as to predict the elective replacement time [16,18]. Generally, follow-up should be every 6 or 12 months, and during the time interval between two follow-ups no information on the pacemaker's functioning may be known. Moreover, the patients do not have any feedback on the actual functioning of the device; this is known to have a psychological impact on patients' life (sometimes with devastating consequences), since they perceive themselves as having a vital dependence on the correct functioning of the device [16]. In my Master Thesis project, I addressed the problem of gathering long term statistics on pacemaker functioning by designing and implementing a contactless device for pacemaker pulse detection. This is based on a coil sensor, which allows to sense the magnetic field variations due to the pacemaker current pulses, without the need for physical contact with patient's skin. During this year my research activity on this topic focused on the assessment of device performances, and on a modelling attempt for coil response to pacemaker pulses aimed at simplifying the design of such a device. The research activity led to the publication of the paper *"A Contactless Sensor for Pacemaker Pulse Detection: Design Hints and Performance Assessment."* on the journal *Sensors* (MDPI).

  Piezoresistive sensor for muscle contraction – Measurement of muscle contraction is mainly achieved through electromyography (EMG) [19] and is an area of interest for many biomedical applications, including prosthesis control and human machine interface [20,21]. However, EMG has some drawbacks [22], and there are also alternative methods for measuring muscle activity, such as by monitoring the mechanical variations that occur during contraction. During this year I joined a research activity aimed at developing and testing the performances of a new, simple, non-invasive sensor based on force-sensitive resistor (FSR), which is able to measure muscle contraction and also Mechanomyography (MMG), i.e. the little vibrations that occur during muscle contraction [23]. The FSR was statically and dynamically characterized by means of a custom test setup. Also, simultaneous recordings of EMG and FSR sensor from flexor carpi ulnaris where acquired, which showed a very high correlation, demonstrating the possibility to adopt the FSR sensor, in place of the EMG, in prosthesis control. This was also tested by implementing a proportional control for a hand prosthesis using the FSR sensor, which allowed to achieve comparable performances with respect to EMG. The research activity led to the publication of the paper "*A Piezoresistive Sensor to Measure Muscle Contraction and Mechanomyography"* on the journal *Sensors* (MDPI).

Realistic Neuronal Modelling and Simulation – Realistic neuronal modelling aims to simulate neural circuits and systems by replicating their real electrophysiological behaviour even at the microscopic scale, as opposed to other approaches, like neural networks, which try to mimic the structures and the behaviour of neural circuits at a macroscopic level, not taking into account their biophysical properties. The ion channels are the elementary building blocks of neurons, so modelling their behaviour represents a fundamental step towards developing biologically detailed neuron models [24]. Until recently, the most utilised models for voltage-gated ion channels follow the formalism introduced by the seminal works of Hodgkin and Huxley (HH) [25]. However, with the development and improvement of the patch-clamp techniques for voltage-clamp experiments, which led to more detailed measurements and data [26], a number of limitations and inconsistencies arose in reproducing the electrophysiological behaviour of voltage-gated channels with the HH formalism [27,28]. On the other hand, Markov-type kinetic models, which represent an ion channel as a collection of states and a set of transitions between them, proved capable to successfully replicate both electrophysiological and biophysical features of different ion channels [29]. However, this models usually have a considerable number of states and transitions in order to model even the finest non-conducting molecular conformational change, and this make them computationally heavy and less suitable for the simulation of large neurons networks, and even of single neurons [30]. In 2017, Pietro Balbi et al proposed a hybrid approach, which consists of a unifying Markov-type model for all isomers of voltage-gated sodium channels (VGSCs), with a minimal set of states and transitions, in order to be computationally efficient in the simulation of their electrophysiological behaviour while keeping an appropriate level of detail in the description of the different features of VGSCs macroscopic currents [31]. In Markov-type kinetic models the transitions between states are regulated by the transition rates, which play the same role of the reaction rates in chemical reactions, describing the concentrations of states which migrates from a state to another one.
In voltage-gated channels, transition rates show a functional dependency on the neuron membrane potential, generally described as the sum of two sigmoidal functions. So, membrane potential can modulate the channels dynamics by modifying the rates of transitions between states. The functional dependency of every transition rate is parameterized with the parameters of the two sigmoids, which need to be tuned in order to make the model able to accurately describe the macroscopic current of the ion channels of interest. Until now, this has been done through a manual optimization procedure, obtaining astonishing results with a great deal of effort. However, for this modelling and simulation methodology to be reliable (and possibly less burdensome) the development of an automatic optimization procedure is necessary.
I started a collaboration with Dr. Pietro Balbi, based on the agreement (convenzione Quadro) between University of Naples Federico II and Istituti Clinici Scientifici Maugeri S.p.A. SB, and my research activity on this topic first focused on the development of such automatic optimization approach. Since optimization procedures involve a considerable number of simulations, the computation time plays a key role in the feasibility of this approach. Therefore, I started an experimental activity aimed at developing a computationally efficient simulation approach in order to reduce computation time as much as possible. Thanks to the participation to the SIE PhD School "Reliability in electronics", I had the opportunity to join a lesson taught by Dr. Francesco Ferranti on alternative fast methods for simulation and uncertainty quantification of electronic circuits, which are based on the use of Numerical Inversion of Laplace Transform (NILT). Then I established a collaboration with Dr. Ferranti to apply the NILT approach to the simulation of voltage-gated ion channels, and now we are working on the development of an automatic optimisation procedure.

References:

[1] Moradi M,et al. Seed localization in ultrasound and registration to C-Arm fluoroscopy using matched needle tracks for prostate brachytherapy. IEEE Trans Biomed Eng 2012;59:2558−2567.

[2] Weese J et al., Voxel-based 2-D/3-D registration of fluoroscopy images and CT scans for image-guided surgery. IEEE Trans Inf Technol Biomed 1997;1:284−293.

[3] Bifulco P, Cesarelli M, Cerciello T, Romano M., A continuous description of intervertebral motion by means of spline interpolation of kinematic data extracted by video fluoroscopy. J Biomech 2012;45:634−641.

[4] Yamazaki T et al., Improvement of depth position in 2-D/3-D registration of knee implants using single-plane fluoroscopy. IEEE Trans Med Imaging 2004;23:602−612.

[5] Wang J, Zhu L, Xing L. Noise reduction in low-dose X-ray fluoroscopy for image-guided radiation therapy. Int J Radiat Oncol Biol Phys 2009;74637−643.

[6] Cerciello T, Romano M, Bifulco P, Cesarelli M, Allen R., Advanced template matching method for estimation of intervertebral kinematics of lumbar spine. Med Eng Phys 2011;33:1293−1302.

[7] Ma L, Moisan L, Yu J, Zeng T. A dictionary learning approach for Poisson image deblurring. IEEE Trans Med Imaging 2013;32:1277−1289.

[8] Tapiovaara MJ. SNR and noise measurements for medical imaging: II. Application to fluoroscopic X-ray

equipment. Phys Med Biol 1993;38:1761−1788.

[9] Cesarelli M, Bifulco P, Cerciello T, Romano M, Paura L. X-ray fluoroscopy noise modeling for filter design. Int J Comput Assist Radiol Surg 2013;8:269−278.

[10] Cerciello T, Bifulco P, Cesarelli M, Fratini A. A comparison of denoising methods for X-ray fluoroscopic images. Biomed Signal Process Control 2012;7:550−559.

[11] Genovese M, Bifulco P, De Caro D, Napoli E, Petra N, Romano M, Cesarelli M, Strollo AGM. Hardware implementation of a spatio-temporal average filter for real-time denoising of fluoroscopic images. J VLSI 2015;49:114−124.

[12] Schuchert, A.; Lepage, S.; Ostrander, J.J.; Bos, R.J.; Gwechenberger, M.; Nicholls, A.; Ringwald, G. Automatic analysis of pacemaker diagnostic data in the identification of atrial tachyarrhythmias in patients with no prior history of them. Europace 2005, 7, 242–247.

[13] Sack, S.; Mouton, E.; Defaye, P.; Dagres, N.; Wolfhard, U.; Wieneke, H.; Herrmann, J.; Oldenburg, O.; Golles, A.; Erbel, R. AIDA Multicenter Study Group. Automatic Interpretation for Diagnosis Asistance. Improved detection and analysis of sensed and paced events in dual chamber pacemakers with extended memory function. A prospective multicenter trial in 626 patients. Herz 2001, 26, 30–39.

[14] Defaye, P.; Dournaux, F.; Mouton, E. Prevalence of supraventricular arrhythmias from the automated analysis of data stored in the DDD pacemakers of 617 patients: The AIDA study. The AIDA Multicenter Study Group. Automatic Interpretation for Diagnosis Assistance. Pacing Clin. Electrophysiol. 1998, 21, 250–255.

[15] Sampaio, S.M.V.; Craveiro, N.M.; Darrieux, F.; de Oliveira, Í.M.; Scanavacca, M.; Hachul, D. Accuracy of the pacemaker event recorder versus Holter-ECG to detect both symptomatic and asymptomatic ventricular arrhythmias. J. Cardiovasc. Electrophysiol. 2018, 29, 154–159.

[16] Roberts, P.R. Follow up and optimisation of cardiac pacing. Hear 2005, 91, 1229–1234.

[17] Gregoratos, G.; Cheitlin, M.D.; Conill, A.; Epstein, A.E.; Fellows, C.; Freedman, R.A.; Hlatky, M.A.; Naccarelli, G.V.; Saksena, S.; Schlant, R.C.; et al. ACC/AHA Guidelines for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices: Executive Summary—A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Pacemaker Implantation). Circulation 1998, 97, 1325–1335.

[18] Udo, E.O.; van Hemel, N.M.; Zuithoff, N.P.; Barrett, M.J.; Ruiter, J.H.; Doevendans, P.A.; Moons, K.G. Incidence and predictors of pacemaker reprogramming: Potential consequences for remote follow-up. Europace 2013, 15, 978–983.

[19] Basmajian, J.V.; De Luca, C.J. Muscles Alive: Their Functions Revealed by Electromyography, 5th ed.; Williams & Wilkins: Baltimore, MD, USA, 1985; ISBN 068300414X.

[20] Spires, M.C.; Kelly, B.M.; Davis, A.J. Prosthetic Restoration and Rehabilitation of the Upper and Lower Extremity; Demos Medical Publishing: New York, NY, USA, 2013; ISBN 978-1-936287-66-6.

[21] Lobo-Prat, J.; Kooren, P.N.; Stienen, A.H.; Herder, J.L.; Koopman, B.F.; Veltink, P.H. Non-invasive control interfaces for intention detection in active movement-assistive devices. J. Neuroeng. Rehabil. 2014, 11, 168.

[22] Amrutha, N.; Arul, V.H. A Review on Noises in EMG Signal and its Removal. Int. J. Sci. Res. Publ. 2017, 7, 23–27.

[23] Ibitoye, M.O.; Hamzaid, N.A.; Zuniga, J.M.; Abdul Wahab, A.K. Mechanomyography and muscle function assessment: A review of current state and prospects. Clin. Biomech. 2014, 29, 691–704.

[24] Hille B (1992) Ion Channels of Excitable Membranes. Sinauer Associates, Sunderland, MA.

[25] Hodgkin AL and Huxley AF. A quantitative description of membrane current and its application to conduction and excitation in nerve. J. Physiol. 1952; 117: 500-544.

[26] Neher E, Sakmann B. Single-channel currents recorded from membrane of denervated frog muscle fibres. Nature. 1976; 260: 799-802.

[27] Strassberg AF, Defelice LJ. Limitations of the Hodgkin-Huxley formalism. Effects of single-channel kinetics on transmembrane voltage dynamics. Neural Comp. 1993; 5: 843-855.

[28] Meunier C, Segev I. Playing the devil's advocate: is the Hodgkin-Huxley model useful? Trends Neurosci. 2002 Nov; 25 (11): 558-63.

[29] Keynes RD, Elinder F. Modelling the activation, opening, inactivation and reopening of the voltage-gated sodium channel. Proc Biol Sci. 1998 Feb 22; 265(1393): 263-70.

[30] Cannon RC, D'Alessandro G. The ion channel inverse problem: Neuroinformatics meets biophysics. PLoS Comput Biol. 2006; 2(8): e91.

[31] Balbi P, Massobrio P, Hellgren Kotaleski J (2017) A single Markov-type kinetic model accounting for the macroscopic currents of all human voltage-gated sodium channel isoforms. PLoS Comput Biol 13(9): e1005737.

Collaborations:

Western Sydney University, Dr. Gaetano Gargiulo

Aston University, Dr. Antonio Fratini

Istituti Clinici Scientifici Maugeri, Dott. Pietro Balbi

IMT Atlantique, Dr. Francesco Ferranti

4. Products

a. Publications as Journal papers
   - *Andreozzi, E.; Gargiulo, G.D.; Fratini, A.; Esposito, D.; Bifulco, P.; "A Contactless Sensor for Pacemaker Pulse Detection: Design Hints and Performance Assessment.", Sensors 2018 (8), 18, 2715.*
   - *Esposito, D.; Andreozzi, E.; Fratini, A.; Gargiulo, G.D.; Savino, S.; Niola, V.; Bifulco, P.; "A Piezoresistive Sensor to Measure Muscle Contraction and Mechanomyography.", Sensors 2018, 18, 2553.*

5. Conferences and Seminars

No conference participations.

6. Activity abroad

No activity abroad.

7. Tutorship

a. Assistant for:
   - B.Sc. course “Elaborazione di Segnali e Dati Biomedici” held by Prof. Mario Cesarelli (**26 hours**)
   - M.Sc. course “Computer Interfaces for Biological Systems” (**8 hours**)
   - M.Sc. course “Strumentazione Biomedica”, held by Prof. Paolo Bifulco (**6 hours**).

b. Master of Science co-supervisor:
   - I assisted Davide Vitiello (supervisor Prof. Paolo Bifulco), during the research activities for his Master Thesis in Biomedical Engineering entitled: “Study of a novel sensor to measure muscle contraction for the control of a hand prosthesis”.
   - I assisted Rosalinda Iodice (supervisor Prof. Mario Cesarelli), for her Master Thesis in Biomedical Engineering entitled: “Realistic Neuronal Simulation: Problem analysis and use of NEURON simulation software”. I introduced her the main topic and the software NEURON, and I reviewed her Master Thesis manuscript.