Hybrid Microfluidic CMOS Sensing Platforms for Life Science Applications

Ebrahim Ghafar-Zadeh, Sebastian Magierowski

- **Motivation and Focus:**

Recent advances in micro- and nanotechnologies have enabled the development of High-Throughput Screening (HTS) techniques for various applications including drug discovery [1]. Owing to the seminal advances in micro-fabrication technologies, HTS is moving towards massively parallel, miniaturized, and label-free platforms. A state-of-the-art DNA sequencing platform featuring millions of Ion-Selective Field Effect Transistors (ISFETs) has convincingly demonstrated the advantage of using standard microelectronic technologies such as Complementary Metal Oxide Semiconductor (CMOS) process in HTS applications [2].

Similarly, many researchers have addressed the challenge of developing HTS systems for monitoring cellular activities on a single chip. Due to the significant advantages of CMOS-based biosensors, such as non-invasive long term recordings, fast response times and label-free processes, they have been widely applied in many biological and medical fields concerning the study of living-cell samples such as neural cell recording and stimulation [3–6], monitoring metabolic activity [7], cell manipulation [8, 9], and extracellular pH monitoring [10,11], nanopore DNA sequencing [16-17] and NMR spectroscopy [18-19].

Among various CMOS sensing techniques, we have reported the advantages of capacitive sensors as low-complexity, high precision, label- free sensing methods for monitoring cellular activities such as cell viability, proliferation and morphology [1, 12, 13]. Also, we investigated the advantages of nano-pore and pH ISFET sensors for DNA sequencing [16 which have revolutionized DNA sequencing technologies. Furthermore, we elaborate on the nuclear magnetic resonance (NMR) sensors a non-invasive method for drug discovery.

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[15] G. Nabovati, E. Ghafar-Zadeh, A. Letourneau, M. Sawan Towards High Throughput Cell Growth Screening: A New CMOS 8 × 8 Biosensor Array for Life Science Applications, IEEE Transactions on Biomedical Circuits and Systems, vol. 11, no.2, pp. 380 - 391, 2017.

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- ## Speakers
  1. Ebrahim Ghafar-Zadeh (EGZ), P.ENG, Ph.D., Associate Professor, York University
  2. Sebastian Magierowski (SM), P.ENG, Ph.D., Associate Professor, York University

- ## Basic Structure

1. **Introduction** An overview of CMOS biosensors and their applications and Post-CMOS Microfluidic Processes will be provided.
2. **CMOS Capacitive Sensor**
   The design and implementation of capacitive sensing techniques including Charge based measurement method (CBCM) will be discussed.
3. **Nano-pore Techniques**
   The principle and application on Nanopore Sensors for various applications including DNA sequencing will be discussed.

Time	Topic	Speaker
1:30 -1:55 pm	1	EGZ
1:55-2:55 pm	2	EGZ
2:55-3:05pm	Break	Break
3:05-4:30pm	3	SM

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CURRENT OCCUPATION

ASSOCIATE PROFESSOR | DEPT. OF EECS| LASSONDE SCHOOL OF ENGINEERING | YORK UNIVERSITY

- Director of Biologically Inspired Sensors and Actuators (BioSA)
- Research Focus: Integrated CMOS/Microfluidics for Cellular Monitoring Applications

DEGREES

Ph.D. | ELECTRICAL ENGINEERING | 2008 | ECOLE POLYTECHNIQUE | MONTREAL | CANADA

M.SC. | ELECTRICAL ENGINEERING | 1997 | UNIVERSITY OF TEHRAN | TEHRAN | IRAN

B.SC. | ELECTRICAL ENGINEERING | 1994 | K.N.T UNIVERSITY | TEHRAN | IRAN

SELECTED PEER-REVIEWED PUBLICATIONS | 15 OUT OF 106

1) ZP. Wu, K. Hammad, E. Ghafar-Zadeh, S. Magierowski, FPGA-Accelerated 3rd Generation DNA Sequencing" IEEE Transactions on Biomedical Circuits and Systems, Accepted, 2019, (Impact Factor: 4.2). 2
2) . Panahi, A. Shomali, M.H. Sabour, E. Ghafar-Zadeh, Molecular Dynamics Simulation of Electric Field Driven Water and Heavy Metals Transport through Fluorinated Carbon Nanotubes,Journal of Molecular Liquids Accepted, Jan. 14, 2019, (Impact Factor: 4.513)
3) S. Hadian-Ghazvinia, H. Ghourchiana, S. Agahb, E. Ghafar-Zadeh, A silver(I) doped bud-like DNA nanostructure as a dual-functional nanolabel for voltammetric discrimination of methylated from unmethylated genes, Journal of Microchimica-Acta (Impact Factor: 5.705)(2019) 186: 384.
4) S Forouhi, R Dehghaniand, E Ghafar-Zadeh, Toward High Throughput Core-CBCM CMOS Capacitive Sensors for life Science Applications: A Novel Current Mode High Dynamic Range Circuitry, Accepted, October 2018, Sensor MDPI
5) G. Nabovati, E. Ghafar-Zadeh et al., Smart Cell Culture Monitoring and Drug Test Platform Using CMOS Capacitive Sensor Array, IEEE Transactions on Biomedical Engineering (Impact Factor: 4.2), Accepted, Aug. 12th, 2018, (id: TBME-00516-2018.R1).
6) G. Nabovati, E. Ghafar-Zadeh, M. Sawan, Towards High Throughput Cell Growth Screening: A New CMOS 8×8 Biosensor Array for Life Science Applications, IEEE Transactions on Biomedical Circuits and Systems, Accepted, June, 2016 (^Manuscript ID: TBioCAS-2015-Dec-0287-Reg.R1).
7) H. Pourmodheji, E. Ghafar-Zadeh, S. Magierowski, A Multidisciplinary Approach Towards High Throughput Nuclear Magnetic Resonance Spectroscopy, Sensors, 16(16), 850-868, 2016.
8) G. Nabovati, E. Ghafar-Zadeh, G. Ayala, M. Mirzaiee, F. Awwad, M. Sawan, A New Fully Differential CMOS Capacitance to Digital Converter for Lab-on-Chip Applications, IEEE Transactions on Biomedical Circuits and Systems, 9(3), 353- 361, 2014.
9) E. Ghafar-Zadeh, Wireless Integrated Biosensors for Point-of-Care Diagnostic Applications, Sensors, 9(3), 353- 361, 20.

BioSA

Biologically-Inspired Sensors and Actuators Laboratory

CV: Sebastian Magierowski (PI)

I. Education and Professional Record

i) Undergraduate

Bachelor of Applied Science in Electrical Engineering
University of Windsor, Department of Electrical Engineering, Windsor, Canada, May 1994

ii) Graduate

Master of Applied Science in Electrical Engineering
University of Toronto, Department of Electrical and Computer Engineering, Toronto, Canada, June 1997

Doctor of Philosophy in Electrical Engineering
University of Toronto, Department of Electrical and Computer Engineering, Toronto, Canada, June 2004

iii) Other Special Training

Licensed Professional Engineer
Association of Professional Engineers, Geologists and Geophysicists of Alberta, April 2006

II. Academic and Other Appointments

Associate Professor ……(January 2013 – Present)
Department of Electrical Engineering & Computer Science, York University
- Research in integrated circuits and embedded computing for biomedical systems
- Developing high-speed DNA sequencing signals and systems

Associate Professor ……(April 2011 – December 2012)
Department of Electrical & Computer Engineering, University of Calgary
- Research in integrated circuits (65/90/130 nm CMOS), embedded computing, wireless systems
- Developed multi-Gbps on-chip oscilloscope for high-speed non-invasive IC testing
- Developed integrated circuits for low-power cooperative wireless communications

Assistant Professor ……(January 2004 – March 2011)
Department of Electrical & Computer Engineering, University of Calgary
- Research in integrated circuits, embedded computing, and wireless systems
- Achieved first demonstration of millimeter wave CMOS parametric integrated circuits

Co-Founder/Mixed-Signal Designer……...(October 1999 – September 2001)
Protolinx Corp., Toronto, Ontario, Canada
- Co-founded high-speed wireless network start-up with technical and business team
- Introduced new wireless communication network based on smart-antenna systems

Mixed-Signal Design Engineer……(May 1999 – September 1999)
PMC-Sierra, Burnaby, British Columbia, Canada
- Designed radio-frequency (RF) microelectronic circuits for internet switches

Research Engineer……(January 1998 – May 1998)
Nortel Networks, Ottawa, Ontario, Canada
- Modeling of MOS transistors for radio-frequency (RF) applications

III. Graduate Supervision and Training

- 12 Graduate students currently under supervision/co-supervision (9 Ph.D., 3 Master's)
- 19 Graduate students graduated under supervision/co-supervision
- Student training and research: **1)** Semiconductor device design, **2)** analog CMOS circuit design, **3)** RF CMOS circuit design, **4)** custom digital ASIC design, **5)** wireless communication system analysis, **6)** on-wafer probing, **7)** test and verification
- Tools: *Cadence* (Virtuoso/Spectre/Encounter/RTL-C/Allegro), *Synopsys* (Sentaurus, VCS, DC, IC Compiler, PrimeTime, Processor Designer, Virtualizer), *Agilent* ADS, *Coventor, Xilinx, Altera*

IV. Research Support

- **Select Federal**
  - Natural Science and Engineering Research Council (NSERC) Discovery Grant ($355k since 2004) - NSERC Collaborative Research Development ($85k since 2012)
  - CMC Integrated Circuit Fabrication Support ($81 since 2004)
  - Canada Foundation for Innovation New Opportunities Grant ($625k since 2005)
- **Select Provincial**
  - Alberta Education and Technology (AET) Small Equipment Grant Program: ($160k since 2011)
  - Alberta Ingenuity Foundation New Faculty Grant ($110k)
- **Select Industrial**
  - Gennum Corp. On-Chip Oscilloscope ($60k)

V. Research and Publications

- Research focused on high-performance integrated CMOS system development (130/90/65-nm)
- Focus on a wireless and embedded system with an emphasis on biomedical systems
- 31 journal, 53 conferences, 3 patent, 1 book chapter publications

A. Select Journals

31. I. Dey, G.G. Messier, and S. Magierowski, "Average Error Rates and Achievable Capacity in Large Office Indoor Wireless Environments," *IEEE Trans Comm*, vol. 65, no. 11, pp. 4955-4965, Nov. 2017.
30. E. Ghafar-Zadeh, G. Ayala-Charca, B. Gholamzadeh, S. Ghasemi, and S. Magierowski, "Towards Scalable Capacitive Cantilever Arrays for Emerging Biomedical Applications" *Sensors and Actuators A: Physical*, vol. 260, pp. 90-98, June 2017.
29. H. Pourmodheji, E. Ghafar-Zadeh, and S. Magierowski, "A CMOS Differential Receiver Dedicated to Nuclear Magnetic Resonance Applications" *Journal of Analog Integrated Circuits and Signal Processing*, vol. 91, no. 1, pp. 97-109, April 2017.
28. K. Dorling, J. Heinrichs, G.G. Messier, and S. Magierowski, "Vehicle Routing Problems for Drone Delivery," *IEEE Trans Sys, Man, and Cyber: Sys*, vol. 47, no. 1, pp. 70-85, Jan. 2017.
27. S. Magierowski, Y. Huang, C. Wang, and E. Ghafar-Zadeh, "Nanopore-CMOS Interfaces for DNA Sequencing" *Biosensors*, 6(3), 42; doi:10.3390/bios6030042, pp. 1-28, Aug. 2016.
26. H. Pourmodheji, E. Ghafar-Zadeh, and S. Magierowski, "A Multidisciplinary Approach Towards High Throughput Nuclear Magnetic Resonance Spectroscopy" *Sensors*, 16(6), 850; doi:10.3390/s16060850, pp. 1-18, June 2016.
25. I. Dey, G.G. Messier, and S. Magierowski, "On the Capacity of Joint Fading and Two-Path Shadowing Channels," *IEEE Trans Vehicular Tech*, vol. 65, no. 1, pp. 403-408, Jan. 2016.
24. S. Magierowski and G.G. Messier, "Internal Readout System for Molecular Recorders," *IEEE Transactions on Molecular, Biological, and Multi-scale Communications*, vol. 1, no. 1, pp. 26-36, Nov. 2015.
23. K. Dorling, G.G. Messier, S. Valentin, and S. Magierowski, "Minimizing the Net Present Cost of Deploying and Operating Wireless Sensor Networks," *IEEE Transactions on Network and service Management*, vol. 12, no. 3, pp. 511-525, sept. 2015.

B. Select Conferences

53. G. Ayala-Charca, E. Ghafar-Zadeh, G. Zoidl and S. Magierowski, "A New Cell-on-Chip Impedometric Interface: Design, Implementation and Experimental Results," *IEEE 60th International Midwest Symp. on Circuits and Sys. (MWSCAS 2017)*, Boston, USA, Aug. 2017, pp. 1-4.
52. R. Hossain, R. Mittmann, E. Ghafar-Zadeh, G. Messier, and S. Magierowski, "GPU Base Calling for DNA Strand Sequencing," *IEEE 60th International Midwest Symp. on Circuits and Sys. (MWSCAS 2017)*, Boston, USA, Aug. 2017, pp. 1-4.
51. N. Mohaghegh, E. Ghafar-Zadeh, S. Munidasa, and S. Magierowski, "Toward Age-related Macular Degeneration (AMD) Big Data: Hardware and Software Design and Implementation," *Proceedings of the 30th IEEE Canadian Conference on Electrical and Computer Engineering (CCECE 2017)*, Windsor, Canada, May 2017, pp. 1-4.
50. C. Wang, Z. Wu, E. Ghafar-Zadeh, S. Magierowski, "Embedded CMOS Bioinformatics for Nanopore Sequencers," *Proceedings of the 30th IEEE Canadian Conference on Electrical and Computer Engineering (CCECE 2017)*, Windsor, Canada, May 2017, pp. 1-4.