Guest Editorial Special Issue on Microfluidics Engineering for Point-of-Care Diagnostics

THE world of biomedical devices is certainly one industrial sector that could benefit the most from microfluidics point-of-care (POC) based diagnostics. Nowadays it is well-known the potential of the POC devices to lead the shift toward the predictive, personalized and preemptive medicine. The idea behind POC devices is to perform a diagnostic test near the patient without the need of any infrastructure and trained personnel. That entails the miniaturization of complex fluids handling, from the single cell to the multi-phase flow, sample manipulation and integrated detection.

The scope of this special issue was to bring together contributions focusing on new concepts in POC devices realization and investigate on their applications. In the **13** papers selected a wide range of methodological and technological solutions are presented: from the sample preparation to the sample manipulation, detection and control. The topics covered are outlined below.

I. POC Devices for Sample Preparation

In "Droplet Size-Aware and Error-Correcting Sample Preparation using Micro-Electrode-Dot-Array Digital Microfluidic Biochips", *Li et al.* present a next generation digital microfluidic biochips platform for precise sample preparation in which the fine-grained control of droplet sizes and real-time droplet sensing is improved.

In "An Enclosed Paper Microfluidic Chip as a Sample Pre-Concentration Based on Ion concentration Polarization", *Liu et al.* developed an enclosed paper-based microfluidic pre-concentrator system based on the ion concentration polarization effect which minimizes sample evaporation, reduced contamination risk, and increased the mechanical strength of the paper channel.

The blood is one of the most common used sample. In "Blood Quality Diagnostic Device Detects Storage Differences Between Donors", *Jani et al.* report the detection of blood biochemical and biophysical changes via 5 μm micrometer blood filtration. The authors show that filterability is highly and more sensitive to changes in blood quality than conventional methods, and that metabolic and deformability changes are correlated with the transfusion quality.

Digital Object Identifier 10.1109/TBCAS.2017.2779279

II. Sample Manipulation Based on Hydrodynamic and Viscoelastic Forces

These papers provide a set of POC solutions, referred as passive devices, in which the sample manipulation is obtained by how the design of a chip geometry affects the flow.

"Double-Mode Microparticle Manipulation by Tunable Secondary Flow in Microchannel with Arc-Shaped Groove Arrays" by *Zhao et al.* proposes a microchannel with an arc-shaped groove structure for micro-particles manipulation into different equilibrium positions through the modulation of the Reynolds number.

"Tapered Microfluidic for Continuous Micro-Object Separation based on Hydrodynamic Principle" by *Ahmad et al.* presents a microfluidic device with a tapered channel to sort particles or cells by size using the hydrodynamic principle coupled with the sedimentation effect. The system was tested on polystyrene microbeads and HeLa cells.

In "High-throughput Separation of White Blood Cells from Whole Blood using Inertial Microfluidics" *Zhang et al.* describe a continuous, high-throughput separation platform that utilizes differential inertial focusing of particles in symmetric serpentine microchannels sorting white blood cells from blood.

In "Continuous Sheathless Separation of White Blood Cells from Whole Blood using Viscoelastic Effects" by *Tan et al.*, the flowing blood sample separation in white and red blood cells is achieved passively thanks to the viscoelastic fluid properties in a microchannel with a two stages bifurcation geometry.

III. Sample Manipulation Based on Impedance Flow Cytometry

These papers show a set of POC solutions in which the sample manipulation is driven by electrophoretic and dielectrophoretic (DEP) forces. This technology allows the cells detection, counting, and sorting by their interaction with an electric field.

"Miniaturaized Impedence Flow Cytometer: Design Rules and Integrated Readout" by *Carminati et al.* describes an high-performance dual-channel, credit-card-sized impedance flow cytometry: from the design of the sensing electrode and cells detection circuit in FPGA to system prototype and the cells manipulation by DEP. The system was tested on polystyrene microbeads and yeast cells (*Saccharomyces Cerevisiae*).

In "Distinct Motion of GFP-Tagged Histone Expressing Cells under AC Electrokinetics in Electrode-Multilayered

Microfluidic Device" *Yao et al.* present the investigation of the motion of *Histone-GFP* type cells, together with *Wild* type cells and *GFP* type cells with the same size but different electrical properties using an electrode-multilayered microfluidic device. Numerical analysis of electrokinetic forces on the cells was conducted and verified by the experimental results.

"ClotChip: a Microfluidc Dielectric Sensor for Point-of-Care Assessment of Hemostasis" by *Maji et al.* proposes the design, fabrication, and testing of a low cost disposable device based on a capacitive sensor for the analysis of blood coagulation process.

In "Characterization of Off-Stoichiometry Thiol-ene Microfluidics Devices for Bioanalytical Applications" by *De Campos et al.*, the Off-Stoichiometry Thiol-ene (OSTE) polymer was used to realize an impedance-based cells counter device based. The system was tested considering the $\alpha-amilase$ surface immobilization and the yeast cells flow counting (*Saccharomyces Cerevisiae*).

IV. Actuation and Control in POC Devices

In "A Surface Acoustic Wave Pumped Lens-less Microfluidic Imaging System for Flowing Cell Detection and Counting" *Huang et al.* describe a device that integrates a pump system based on surface acoustic wave (SAW) technology for the flow actuation with CMOS lens-less microfluidic imaging system for flowing cells detection and counting. A motion detection algorithm was utilized for continuously flowing cells characterization. The system was tested on human bone marrow stromal cells flow.

"Pressure-Aware Control Layer Optimization for Flow-Based Microfluidic Biochips" by *Wang et al.* copies with the challenge of control system design for flow based microfluidics. An algorithm for an optimal control of a multiplexer layer driving the valves switching is presented with a double aim: to minimize the switch-over time of the multiplexer from one state to another and to prevent accidental actuation of valves through pressure degradation.

The 50% of the papers received were selected based on technical reviews from worldwide experts to offer the best landscape in this field. For that the Guest Editors would like to thank all the authors and reviewers. We also owe our deepest thanks to Prof. M. Sawan, Editor-in-Chief of IEEE Transactions on Biomedical Circuits and Systems, for his constant support.

M. Bucolo, *Guest Editor*
University of Catania
Catania 95124, Italy

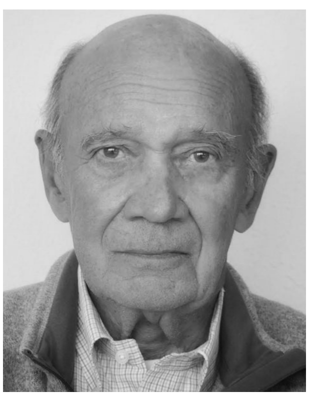
J. Guo, *Guest Editor*
University of Electronic Science and Technology of China
Chengdu 610051, China

M. Intaglietta, *Guest Editor*
University of California San Diego
San Diego, CA 92093 USA

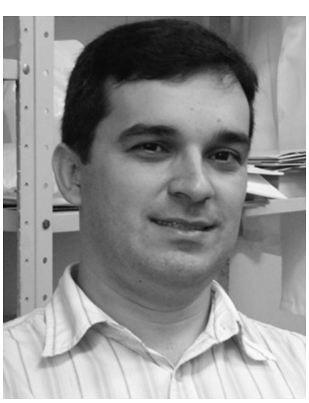
W. K. T. Coltro, *Guest Editor*
Federal University of Gois
Goiânia, GO 74690-900, Brazil

Maide Bucolo (SM'09) received the M.S. degree in computer science engineering in 1997, and the Ph.D. degree in electronic and control engineering in 2001 from the University of Catania, Catania, Italy. During the Ph.D. degree, she was a Research Scholar with the University of California San Diego, San Diego, SA, USA (UCSD) and after that, often, she was a Visiting Researcher with Microhemodynamics Lab of the Department of Bioengineering, UCSD. She is currently an Associate Professor in control system with the Department of Electrical, Electronic, and Informatics, University of Catania. Her research interests include methodologies and low-cost technologies for bio-microfluidics systems modeling and control. In 2010, she established and became responsible of the "Bio-Microfluidics Laboratory" (http://www.dees.unict.it/mbucolo/index.php/resources). She was the Coordinator of National Projects and International Exchange Programs. She was an Expert in the technology innovation demand of regional small and medium enterprisers. She has authored or coauthored more than 100 scientific contributions in peer-reviewed international journals and conferences.

Jinhong Guo received the Bachelor's degree in electronic engineering from the University of Electronic Science and Technology of China, Chengdu, China, in 2010 and the Ph.D. degree in biomedical engineering from the Nanyang Technological University, Singapore, in 2014. He is currently a Full Professor with the School of Communication and Information Engineering, University of Electronic Science and Technology of China, Chengdu, China. After his doctoral studies, during 2014–2015, he was a Postdoctoral Fellow in the Pillar of Engineering Design with MIT-SUTD, Singapore. From January 2016 to July 2016, he was a Visiting Professor with the School of Mechanical Engineering, University of Michigan, Ann Arbor, MI, USA. His current research interests include electrochemical sensor and lab-on-a-chip devices for point of care test toward clinical use. He received the China Sichuan Thousand Talents Plan for Scholars Award (2015) and Chengdu Expert in Science and Technology Award (2015). He is also appointed as the Chief Scientist at Longmaster Information Co., Ltd (one listed corporation in China, stock ID: 300288), who is in charge of the research and development center for POCT. He has authored or coauthored 70 publication in top journal, such as IEEE TII, Analytical Chemistry, Biosensor, and Bioelectronics, etc.



Marcos Intaglietta was born in Buenos Aires, Argentina. He received the B.S. degree in mechanical engineering from the University of California, Berkeley, Berkeley, CA, USA, in 1977, and the M.S. and Ph.D. degrees in mechanical engineering and applied mechanics from the California Institute of Technology, Pasadena, CA, USA, in 1959 and 1964, respectively. From 1964 to 1966, he was an Established Investigator of the Los Angeles County Heart Association. He was an Assistant Professor of Applied Mechanics and Bioengineering with the Department of Applied Mechanics and Engineering Science, University of California San Diego, San Diego, USA, in 1966, an Associate Professor in 1971 and a Full Professor in 1976. He developed methods for in-vivo measurements of micro flow, pressure, vessel dynamics, micro pO2 and NO, and capillary function in in the microcirculation of the unanesthetized hamster chamber window. Since 1980, he studies the micro-tissue effects of blood transfusion and develops alternatives to using blood in treating blood loss and anemia. He is the Author of 364 peer reviewed publications (PubMed), and a total of 499 publications including book chapters, books, and patents.



Wendell K. T. Coltro received the B.Sc. degree in chemistry from the State University of Maringa, Maringa, Brazil, in 2002. He received the M.Sc. and Ph.D. degrees in analytical chemistry from the University of São Paulo, São Paulo, Brazil, under the mentoring of Prof. E. Carrilho, from the Institute of Chemistry at São Carlos, in 2002 and 2008, respectively. In 2006, he was a Visiting Scholar with the University of Kansas Lawrence, KS, USA, under the supervision of Prof. S. Lunte. He is currently an Associate Professor of analytical chemistry with the Federal University of Goias, Goiânia, Brazil. His research interests include instrumental advances for applications in electrophoresis chips, electrochemical sensors, development of toner- and paper-based devices for bioanalysis, clinical diagnostics and microfabrication techniques based on 3-D printing and alternative approaches for laboratories with limited resources.