Special Session: Design of Microfluidic Biochips: Connecting Algorithms and Foundations of Chip Design to Biochemistry and the Life Sciences

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Abstract

Advances in microfluidic technologies have led to the emergence of biochip devices for automating laboratory procedures in biochemistry and molecular biology. Corresponding systems are revolutionizing a diverse range of applications, e.g. air quality studies, point-of-care clinical diagnostics, drug discovery, and DNA sequencing—with an increasing market. For clinical diagnostics, it has been predicted that we will soon see 15 billion diagnostic tests per year worldwide.

However, continued growth (and larger revenues resulting from technology adoption by pharmaceutical and healthcare companies) depends on advances in chip integration and design-automation tools. Thus, there is a need to deliver the same level of Computer-Aided Design (CAD) support to the biochip designer that the semiconductor industry now takes for granted. In particular, these CAD tools will adopt computational intelligence for the optimization of biochip designs. Also, the design of efficient CAD algorithms for implementing biochemistry protocols to ensure that biochips are as versatile as the macro-labs that they are intended to replace. This is therefore an opportune time for the software and semiconductor industry as well as circuit/system designers to make an impact in this emerging field.

The session will consist of four talks on complementary aspects of these emerging technologies. The speakers will describe emerging technologies for integrated microfluidics, including synthesis, chip-level optimization, fault-tolerance design, and sample preparation applications. We believe that the special session will generate interest in this topic, leading to more research, aiming at delivering complete EDA tool-flows for this emerging area.

Organizers’ Biographies

Tsung-Yi Ho received his Ph.D. in Electrical Engineering from National Taiwan University in 2005. He is a Professor with the Department of Computer Science of National Tsing Hua University, Hsinchu, Taiwan. From 2007 to 2014 and 2015, he was with National Cheng Kung University and National Chiao Tung University, respectively. His research interests include design automation and test for microfluidic biochips and nanometer integrated circuits. He has presented 8 tutorials and contributed 8 special sessions in ACM/IEEE conferences, all in design automation for microfluidic biochips. He has been the recipient of many research awards, such as Dr. Wu Ta-You Memorial Award of National Science Council (NSC) of Taiwan, Junior Research Investigators Award of the Academia Sinica, Distinguished Young Scholar Award of the Taiwan IC Design Society, Outstanding Young Electrical Engineer Award of the Chinese Institute of Electrical Engineering, the Delta Electronics K.T. Li Research Award, the ACM
Taipei Chapter Young Researcher Award, the IEEE Tainan Chapter Gold Member Award, the Invitational Fellowship of the Japan Society for the Promotion of Science (JSPS), the Humboldt Research Fellowship by the Alexander von Humboldt Foundation, and the Hans Fischer Fellow by the Institute of Advanced Study of the Technical University of Munich. He was a recipient of the Best Paper Awards at the VLSI Test Symposium (VTS) in 2013 and *IEEE Transactions on Computer-Aided Design of Integrated Circuits and Systems* in 2015. He currently serves as an ACM Distinguished Speaker, a Distinguished Visitor of the IEEE Computer Society, the Chair of the IEEE Computer Society Tainan Chapter, the Chair of the ACM SIGDA Taiwan Chapter, and Associate Editor of the *ACM Journal on Emerging Technologies in Computing Systems* and *IEEE Transactions on Computer-Aided Design of Integrated Circuits and Systems*, *IEEE Transactions on Very Large Scale Integration Systems*, Guest Editor of *IEEE Design & Test of Computers*, and the Technical Program Committees of major conferences, including DAC, ICCAD, DATE, ASP-DAC, ISPD, ICCD, etc.

**Shigeru Yamashita** is a professor of Department of Computer Science, College of Information Science and Engineering, Ritsumeikan University. He received his B. E., M. E. and Ph.D. degrees in information science from Kyoto University, Kyoto, Japan, in 1993, 1995 and 2001, respectively. His research interests include new types of computation and logic synthesis for them. He received the 2000 IEEE Circuits and Systems Society Transactions on Computer-Aided Design of Integrated Circuits and Systems Best Paper Award, SASIMI 2010 Best Paper Award, 2010 IPSJ Yamashita SIG Research Award, and 2010 Maruban Academic Achievement Award of the Marubun Research Promotion Foundation. He is a senior member of IEEE and IEICE, and a member of IPSJ.

**Ansuman Banerjee** is currently an Associate Professor at the Advanced Computing and Microelectronics Unit, Indian Statistical Institute Kolkata. His research interests include design automation for embedded systems, hardware/software verification, CAD, and automata theory. Specifically, his research objective is focused on developing tools, techniques and methodologies for specification analysis, automated software debugging, functional test generation and formal/semi-formal verification for embedded systems. Ansuman received his B.E. from Jadavpur University, and M.S. and Ph.D. degrees from the Indian Institute of Technology Kharagpur -- all in Computer Science. Ansuman has spent about 6 months at the National University of Singapore as a research fellow working in software engineering and about 4 years at Interra Systems India Pvt. Ltd. (a software company) in various roles.

**Sudip Roy** is currently an Assistant Professor in the Department of Computer Science and Engineering of Indian Institute of Technology (IIT) Roorkee, India. He received his B.Sc. (honors) degree in Physics and B.Tech. degree in Computer Science and Engineering from the University of Calcutta, Kolkata, India, in 2001 and 2004, respectively, the M.S. (by research) and Ph.D. degrees in Computer Science and Engineering from the Indian Institute of Technology (IIT) Kharagpur, India, in 2009 and 2014, respectively. His research interests include electronic design automation (EDA) of microfluidic lab-on-a-chips and digital VLSI integrated circuits. He has published several research articles on EDA for digital microfluidic lab-on-a-chips. He has published in 10 peer-reviewed journals and 19 international conferences in the aforementioned areas. He has authored one book, one book chapter, one US patent and filed two US patents.

### Contributed Presentations in the Special Session

**The Coming of Age of Microfluidics: EDA Solutions for Enabling Biochemistry on a Chip**

**Tsung-Yi Ho**

*Abstract:* This talk offers attendees an opportunity to bridge the semiconductor ICs/system industry with the biomedical and pharmaceutical industries. This talk will first describe emerging applications in biology and biochemistry that can benefit from advances in electronic “biochips”. The presenter will next describe technology platforms for accomplishing “biochemistry on a chip”, and introduce the audience the droplet-based "digital" microfluidics based on electrowetting actuation. Next, the presenter will describe system-level synthesis includes operation scheduling and resource binding algorithms, and physical-level synthesis includes placement and routing...
optimizations. In this way, the audience will see how a “biochip compiler” can translate protocol descriptions provided by an end user (e.g., a chemist or a nurse at a doctor’s clinic) to a set of optimized and executable fluidic instructions that will run on the underlying microfluidic platform. The problem of mapping a small number of chip pins to a large number of array electrodes will also be covered. Finally, sensor feedback-based cyberphysical adaptation will be covered.

**Pin-Count Reduction Techniques for Logic Integrated Digital Microfluidic Biochips**
*Shigeru Yamashita*

**Abstract:** Digital microfluidic biochips have become one of the most promising technologies for biomedical experiments. For digital microfluidic biochips, reducing the number of independent control pins that reflects most of the fabrication cost, power consumption and reliability of a microfluidic system. Thus, there have been many challenges to reduce the number of control pins. However, most of the previous pin-count reduction techniques cannot guarantee the same completion time of the original design without the pin-count reduction.

By integrating a very simple combinational logic circuit, we can design a digital microfluidic biochip with an information-theoretic minimum number of control pins without increasing the completion time. In this talk, we explain this idea and present some techniques to reduce the number of control pins for application-specific as well as general-purpose digital microfluidic biochips.

**Correctness Checking of Bio-chemical Protocol Realizations on a Digital Microfluidic Biochip**
*Ansuman Banerjee*

**Abstract:** Recent advances in digital microfluidic (DMF) technologies offer a promising platform for a wide variety of bio-chemical applications, such as DNA analysis, automated drug discovery, and toxicity monitoring. For on-chip implementation of complex bioassays, automated synthesis tools are now being used in order to meet the increasing design challenges. Currently, the synthesis tools cycle through a number of complex design steps to realize a given bio-chemical protocol on a target DMF architecture. Thus, several design errors are likely to creep into the synthesis process. Before deploying a DMF biochip on a safety critical system, it is becoming mandatory to ensure that the desired bio-chemical protocol has been correctly implemented, i.e., the synthesized output (actuation sequences for the biochip) is free from any design or realization errors. In this session, we discuss a symbolic constraint-based analysis and verification framework for checking the correctness of a synthesized bio-chemical protocol with respect to the original design specification. The discussion will talk about a framework that can detect realization errors and generate diagnostic feedback to indicate the possible sources of design rule violations.

**Computer-Aided-Design (CAD) for Fluidic Sample Preparation using Digital Microfluidic Biochips**
*Sudip Roy*

**Abstract:** During last two decades, an emerging technology of Lab-on-a-Chips (LOCs) or Biochips has been studied by the researchers of interdisciplinary fields to develop microfluidic chips that can implement wide-range of biochemical laboratory test protocols (a.k.a. bioassays). A marriage of microelectronics and in-vitro diagnostics areas has led to this field of interdisciplinary research around LOCs. In contrast to continuous-flow microfluidic chips, digital microfluidic (DMF) biochips are popular microfluidic LOCs that can implement bioassays on an electrode array of a few square centimeters in size by manipulating micro/nano/pico liter volume fluid droplets. The functionality of a DMF biochip includes the following operations: dispensing the desired amount of fluids to the chip from the outside world as droplets, transporting the droplets on-chip to appropriate locations, mixing and splitting of several droplets, executing a well-defined bioassay on a chip, and finally analyzing the results at an on-chip detection site. Recently, computer-aided-design (CAD) techniques have been extensively used for developing DMF biochips. It
is expected that in near future, with the help of CAD techniques, tube and pipette based biochemical laboratory protocols will be revolutionized as small size biochips as the valve and tube based technology for electronic devices has been shifted to today’s semiconductor based very-large-scale-integration (VLSI) chips.

Dr. Sudip Roy’s research envisions the computer-aided-design (CAD) research to develop DMF biochips by designing algorithms for automated sample preparation (dilution and mixing) on such chips. Mixing and dilution of fluids are fundamental preprocessing steps in almost all biochemical laboratory protocols. Mixing of two or more fluids with a given ratio is often required as a preprocessing step of many real-life biochemical protocols, e.g., polymerase chain reaction (PCR). Dilution of a biochemical fluid is the special case of mixing, where only two different types of fluids, one of which is a buffer solution, are mixed at a certain ratio corresponding to the desired concentration. The dilution is commonly used in biological studies to create a variety of concentrations of the stock solution by mixing it with its diluents and it is required for sample preparation in many bioassays, e.g., real-time PCR, immunoassays, etc. For high-throughput applications, it is a challenge to determine the sequence of minimum number of mix-split steps for on-chip sample preparation. Furthermore, the production of waste droplets and/or the reactant fluid usage should be minimized. Moreover, design automation tools are necessary for optimizing the layout of the biochips.

In his talk, he will discuss about some computer-aided-design (CAD) techniques for automatic synthesis of biochips and several CAD techniques for automated and on-chip fluidic sample preparation (dilution and mixing) of biochemical fluids using DMF biochips.