CAD Algorithms for Digital Microfluidic Biochips

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Microfluidic-based biochips are revolutionizing clinical diagnostics and other biochemical laboratory test procedures (also called *bioprotocols* or *bioassays*). One category of microfluidic chips are continuous-flow microfluidic chips, where continuous liquid flow through microfabricated channels is manipulated with the help of micropumps, microvalves, etc. A more versatile category of biochips are digital microfluidic (DMF) biochips, where discrete nano-liter volumes (called *droplets*) of biochemical (or reagent) fluids are manipulated on a substrate of two-dimensional array of electrodes to implement a bioprotocol on a chip of a few square centimeters in size. Basically, the principle of physics that is used in DMF biochips is called electrowetting-on-dielectric (EWOD). In this special phenomenon, a fluid droplet sitting on an electrode in a biochip can be moved to the adjacent electrode by changing its surface tension on applying suitable actuation voltages to the electrodes. Compared to traditional bench-top bioprotocols, DMF biochip technology offers the advantages of low sample and reagent consumption, less likelihood of error due to minimal human intervention, high-throughput and high sensitivity, portability, increased automation, low-power consumption, low-cost and reliability. Performance of such systems depends on the ability to manipulate very small amount (micro/nano/pico litres volume) of fluids quickly and automatically. As each droplet (or group of droplets) can be controlled individually, these types of biochips also have dynamic reconfigurability and architectural scalability. In general, a DMF biochip functionality includes the following operations: measuring and dispensing accurate volume of droplets into the chip from the external reservoirs at the chip boundary, transporting droplets to appropriate locations on-chip, mixing of droplets, splitting of a larger droplet into smaller ones, on-chip detection and analysis of droplet by sensors. A DMF biochip can integrate multiple bioprotocol operations on a single chip. In the first part of this talk, we will discuss about the basics and applications of DMF biochips.

The DMF biochip design-flow follows similar flow as for the digital VLSI chips like *high-level synthesis* (i.e., fluidic operation scheduling of a bioprotocol, microfluidic module selection and assignment to those operations) and *physical design* (i.e., module placements on the 2D array of electrodes and droplet routing). Development of DMF a biochip requires to solve several associated combinatorial and geometric optimization and computer-aided design (CAD) problems. In this talk, next we will discuss about some of the CAD algorithmic problems those are being solved by several research groups.

Since off-chip sample processing and sample preparation pose a significant hindrance to the overall biochemical assay time, for fast and high-throughput applications, sample preprocessing steps should also be automated on-chip, i.e., integrated and self-contained on the biochip itself. Currently, we are working on the CAD problems involved in the automation of on-chip fluid (samples/reagents) preparation of a bioassay. We have proposed an algorithm for automatic dilution of fluid samples on-chip that can reduce the number of waste droplets during sample preparation compared to a recently published work (accepted in *IEEE TCAD* in June, 2010). In this talk, we will briefly discuss about that work.

Have a look on these videos:

[1] Droplet manipulation, Institute for Integrated Micro and Nano Systems, University of Edinburgh.
[2] On-chip droplet mixing, Prof. Aaron Wheeler's research group, University of Toronto.
[3] Some example protocols in action, Advanced Liquid Logic, Inc.

Quick reading on Web:

[1] Programmable Lab on a Chip, Birck Nanotechnology Center, Purdue University.
[2] Wheeler Microfluidics Laboratory, Prof. Aaron Wheeler's research group, University of Toronto.