Droplet Routing Algorithms for Digital Microfluidic Biochips

[Undergraduate]

Tsung-Wei Huang*
Department of Computer Science and Information Engineering
National Cheng Kung University, Tainan, Taiwan

1. PROBLEM AND MOTIVATION

Digital microfluidic biochip (DMFB) is an emerging technology that aims to miniaturize and integrate droplet handling on a chip. Recently, many on-chip laboratory procedures such as immunoassay, real-time DNA sequencing, and protein crystallization have all been successfully demonstrated on DMFBs [5]. Researchers addressed these procedures with architectural-level and physical-level synthesis [3]. In the architectural-level synthesis, the goal is to schedule the assay functions and bind them to a given number of resources so as to maximize the parallelism, thereby decreasing the process time. During the physical-level synthesis, modules of these resources must be placed in the 2D microfluidic array to minimize the entire chip area [4]. Then the droplets must be appropriately routed to perform these prescheduled biological operations (e.g., sample mixing or detection) [6].

As advances in DMFBs, the droplet routing problem has become a key design issue in the physical-level synthesis of DMFBs, which schedules the movement of each droplet in a time-multiplexed manner. This physical synthesis is one of the most critical design challenges due to high complexity as well as large impacts on assay performance. Unlike the traditional VLSI routing, in addition to routing paths decision, the droplet routing problem needs to address the issue of droplet scheduling under the practical constraints imposed by the fluidic property and timing restriction of synthesis results. In this work, droplet routing algorithms are proposed to address the practical issues imposed by routability, contamination, and pin-count reduction.

*Tsung-Wei Huang is a senior student with the Department of Computer Science and Information Engineering, National Cheng Kung University, Tainan 701, Taiwan; email: twhuang@eda.csie.ncku.edu.tw; post-address: No.243, Zhongxing Rd., Shuishang Township, Chiayi County 608, Taiwan (R.O.C.); ACM student member number: #1201105; contest category: undergraduate; His research advisor is Tsung-Yi Ho, with the Department of Computer Science and Information Engineering, National Cheng Kung University, Tainan 701, Taiwan; email: tyho@csie.ncku.edu.tw

2. BACKGROUND AND RELATED WORK

Fig. 1(a) shows the schematic view of a DMFB. A DMFB contains three components, the 2D microfluidic array, the dispensing ports/reservoirs, and the optical detectors. The basic architecture of a DMFB contains a set of basic cells which consist of two parallel glass plates (see Fig. 1(b)(c)). The bottom plate contains a patterned array of individually controllable electrodes, and the top plate is coated with a continuous ground electrode. By independently controlling the voltage of electrodes, droplets can be moved along this line of electrodes due to the principle of electrowetting on dielectric (EWOD) [2]. Therefore, droplet routing supports all the fluidic operation such as mixing and dilution, which plays an important role on DMFBs.

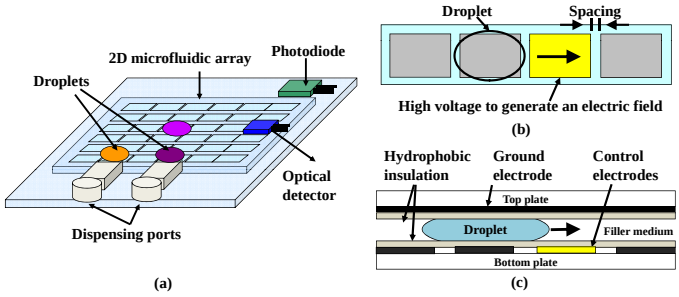

Figure 1: A digital microfluidic biochip (DMFB) [6]. (a) Schematic view of a DMFB. (b) Top view of the 2D microfluidic array. (c) Side view of the 2D microfluidic array.

Droplet routing problem has attracted much attention in the literature recently [1, 6, 10]. These methods consider only local optimization when routing a droplet, which suffers from the routability problem. To tackle the problem, we have published a work in *2009 IEEE International Conference on Computer Design (ICCD'09)* to solve the droplet routing. In many safe-critical designs, contamination problem should be avoided during the droplet routing [7]. In [11], they use disjoint routes algorithm and insert the wash operations between successive subproblems of bioassays. This method suffers from high routing complexity caused by disjoint routes and redundant routing time for wash droplets. To remedy the deficiencies, we have published a contamination aware droplet routing algorithm to handle the scheduling of wash operations in *2009 ACM/IEEE International Conference on Computer Aided Design (ICCAD'09)*. To make the biochip feasible for practical applications, pin-count reduction is a major design problem. However, the solu-

tion of current pin-count aware technique is inevitably limited by simply adopting it after the droplet routing stage, thereby restricting the solution quality [8, 9]. To solve the problem, we propose the first droplet routing algorithm for PDMFBs that can integrate pin-count reduction technique with droplet routing stage, which has been published in *2010 ACM International Symposium on Physical Design (ISPD'10)* .

3. APPROACH AND UNIQUENESS

To handle the droplet routing problem, we propose a fast routability- and performance-driven droplet routing algorithm which has been published in *IEEE ICCD'09*. We first construct the preferred routing tracks to make droplets route orderly on these tracks thereby reducing the design complexity and used cells. To reach better routability, we also introduce an equation that considers the congestion issue of each droplet net globally to determine the routing priority. Finally, a dynamic programming based compaction technique is presented to minimize the routing time.

For safe-critical designs that need avoid the contamination problem, we propose a contamination aware droplet routing algorithm to further coordinate this issue to the droplet routing. This work has been published in *ACM/IEEE ICCAD'09*. We introduce a k-shortest path algorithm to minimize the contaminations caused by the routing. Then, a minimum cost circulation flow (MCC) based algorithm is adopted to optimally solve the scheduling of wash operations within one sub-problem. Furthermore, a look-ahead prediction technique is used to determine the contaminations between successive subproblems. After that, we simultaneously clean both contaminations within one subproblem and those between successive subproblems by using the MCC-based algorithm to reduce the execution time and the used cells significantly.

As the market issue of pin-count reduction, we have published a work in *ACM ISPD'10* that integrates the pin-count reduction with the droplet routing. We first propose a basic ILP formulation that can directly solve the droplet routing problem for pin-constrained DMFBs. Due to the complexity of this ILP formulation, we also propose a two-stage technique of global routing followed by incremental ILP-based routing to reduce the solution space. To further reduce the runtime, we present a deterministic ILP formulation that casts the original routing optimization problem into a decision problem, and solve it by a logarithmic time based search method.

4. RESULTS AND CONTRIBUTIONS

In *ICCD'09*, our routing algorithm achieves 100% routing completion for all bioassays while previous algorithms are not. Furthermore, the experimental results demonstrate that the proposed method can achieve better timing result, fault tolerance and faster runtime. In *ICCAD'09*, the evaluation performed on four widely used bioassays shows the completeness of all bioassays without any contamination problem. Our algorithm outperforms the previous work by achieving faster droplet routing time and better fault tolerance. In *ISPD'10*, extensive experiments demonstrate that in terms of the number of the control pins, the number of the used cells, and the latest arrival time, we acquire much better achievements than all the state-of-the-art algorithms in any aspect. These experimental results demonstrate the efficiency and robustness of our proposed methods which are capable of handling complex droplet routing problem under many practical issues.

These topics can be published in many CAD conferences such as DAC, ICCAD, and ISPD. The related topic is *biologically inspired systems* in the category *New and Emerging Design Technologies*.

5. REFERENCES

[1] M. Cho and D. Z. Pan, "A high-performance droplet routing algorithm for digital microfluidic biochips," *IEEE Trans. on CAD*, vol. 27, no. 10, pp. 1714–1724, Oct. 2008.

[2] M. G. Pollack, A. D. Shenderov, and R. B. Fair, "Electrowetting-based actuation of droplets for integrated microfluidics," *Lab Chip*, vol. 2, no. 2, pp. 96–101, May 2002.

[3] F. Su and K. Chakrabarty, "Architectural-level synthesis of digital microfluidics-based biochips," *Proc. IEEE International Conference on CAD*, pp. 223-228, 2004.

[4] F. Su and K. Chakrabarty, "Unified high-level synthesis and module placement for defect-tolerant microfluidic biochips," *Proc. ACM/IEEE DAC*, pp. 825-830, 2005.

[5] F. Su, K. Chakrabarty, and R. B. Fair, "Microfluidics based biochips: Technology issues, implementation platforms, and design-automation challenges," *IEEE Trans. on CAD*, vol. 25, no. 2, pp. 211–223, Feb. 2006.

[6] F. Su, W. Hwang, and K. Chakrabarty, "Droplet routing in the synthesis of digital microfluidic biochips," *Proc. ACM/IEEE DATE*, pp. 1–6, Mar. 2006.

[7] J. Y. Toon and R. L. Garrell, "Preventing biomolecular adsorption in electrowetting-based biofluidic chips, " *Anal. Chem.*, vol. 75, no. 19, pp. 5097–5102, Oct. 2003.

[8] T. Xu and K. Chakrabarty, "Automated design of digital microfluidic lab-on-chip under pin-count constraints," *Proc. ACM ISPD*, pp. 90–98, Apr. 2008.

[9] T. Xu and K. Chakrabarty, "Broadcast electrode-addressing for pin-constrained multi-functional digital microfluidic biochips," *Proc. ACM/IEEE DAC*, pp. 173–178, Jun. 2008.

[10] P. H. Yuh, C. L. Yang, and Y. W. Chang, "BioRoute: A network flow based routing algorithm for the synthesis of digital microfluidic biochips," *IEEE Trans. on CAD*, vol. 27, no. 11, pp. 1928–1941, Nov. 2008.

[11] Y. Zhao and K. Chakrabarty, "Cross-contamination avoidance for droplet routing in digital microfluidic biochips," *ACM/IEEE DATE*, Apr. 2009.

6. MY PUBLICATIONS

[1] T.-W. Huang and T.-Y. Ho, "A Fast Routability- and Performance-Driven Droplet Routing Algorithm for Digital Microfluidic Biochips," *Pro. of IEEE ICCD*, Oct. 2009.

[2] T.-W. Huang and T.-Y. Ho "Contamination Aware Droplet Routing for Digital Microfluidic Biochip," *Proceedings of International Workshop on Bio-Design Automation*, July, 2009.

[3] T.-W. Huang, C.-H. Lin and T.-Y. Ho, "A Contamination Aware Droplet Routing Algorithm for Digital Microfluidic Biochips," *Pro. of ACM/IEEE ICCAD*, Nov. 2009.

[4] T.-W. Huang and T.-Y. Ho, "A Two-Stage ILP-Based Droplet Routing Algorithm for Pin-Constrained Digital Microfluidic Biochips," *Pro. of ACM ISPD*, Mar. 2010.

[5] T.-W. Huang, C.-H. Lin and T.-Y. Ho, "A Contamination Aware Droplet Routing Algorithm for the Synthesis of Digital Microfluidic Biochips," in revision, *IEEE Trans. on CAD*, 2010.