An Adaptive Low Cost Single Target Sample Preparation on Digital Microfluidic Biochips

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***Abstract*—Sample preparation on Digital Microfluidic Biochips (DMFBs) is an indispensable process for accomplishing biochemical reactions. Original reactants are usually diluted to the solutions with desirable concentrations. Framing various droplets with desired target concentrations on such a chip in an automated manner is the real challenge to sort out. In this work, we propose an Adaptive Sample Preparation Algorithm (ASPA) for DMFB. It can produce any sample droplets within the range of (0-1024) concentration factors (CF's) in an adaptive manner. The proposed method also ensures an error-free, cost-effective sample preparation for Digital Microfluidic Biochip (DMFB). Our method significantly reduces the number of sample droplets to prepare any single target concentration on a DMFB platform while the number of mixing-splitting steps remains the same for most of the cases compared to earlier methods. The requirement of buffer droplets and waste may be slightly more for a few cases in this method. However, as the buffer cost is negligible compared to fluid samples, the overall sample preparation cost decreases by our method.**

***Index Terms*—Digital Microfluidic Biochip, Sample preparation, Reagent, Concentration Factor, Adaptive**

I. INTRODUCTION

Digital Microfluidic Biochips replace the conventional complex biochemical process and also have the power to control the precise nanoscale volume of fluids like the sample, reagent, etc. The droplet can route on a 2-dimensional biochip in a discrete way [1]. DMFB is a new field of interdisciplinary research based on lab-on-a-chip (LoC) called as Total Analysis System(TAS) widely used in healthcare engineering and medical instrumentation domain [2]. Typically, an LoC can perform various biochemical in vitro test protocols (bioassay) on a single chip that is as small as a few square centimeters in size and which can provide low-cost and fast diagnostic solutions. In particular, droplet-based microfluidic biochips have gained wide acceptance in recent times for developing LoC applications in contrast to continuous-flow microfluidic chips. It uses electrical actuation to perform dispensing, transporting, merging, mixing, splitting operations on a droplet. Such a prototype chip has been used for clinical diagnostics, which includes more than 5000 electrodes. A commercial DMFB chip embeds more than 3 lacs of $(20\mu m \times 20\mu m)$ electrodes, acted as an integrated optical detector [3], [4]. The top-view of such a typical DMFB chip is depicted in Fig. 1.

In DMFB Synthesis, two important design optimization issues are in the area of routing [5], and mixing [6] to efficiently accomplish bio-protocols. Sample preparation of desired concentration is part of such bioassays [7] where dilution of a reactant fluid and mixture-preparation of several reactant fluids are two fundamental preprocessing steps. In diagnostic laboratories, off-chip samples are prepared manually and then put into the diagnostic machines which are susceptible to error due to human intervention and other experimental factors and take longer time and lesser throughput in comparison to automated on-chip sample preparation.

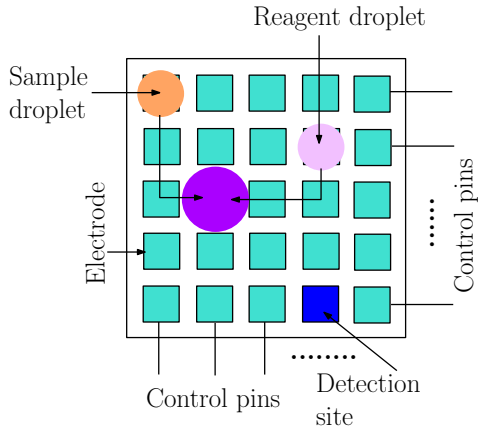

Fig. 1: Top view of a DMFB chip [4]

The majority of biochemical procedures are based on solution preparation. It is a primary step to prepare the sample or reactant at the desired concentration before combining it with another fluid. A biological sample/reagent must be diluted with the help of a buffer solution (called Diluent) to a desired concentration value [8] before mixing with another fluid. For In_Vitro testing, the dilution process has been used repeatedly to arrange different concentration ranges of solutions on a microfluidic device. Furthermore, for an effective bio-protocol, various assay activities (mixing, detection, mixing control, etc.) must be integrated on a single chip [8], [7].

Two types of dilution methods are used till date in DMFB platform. Serial (exponential) dilution and interpolated dilution [9]. A sample or reagent with 100% concentration is mixed with a buffer solution with 0% concentration repeatedly and the concentration of the solution reduces accordingly [8]. Hence, the new concentration factor of the solution is $(C_t = \frac{1}{2^n})$, where the value of n is 10_{10} and T_{ms} is denoted as the number of mix-split steps [9], [8]. Two equal shape and volume droplets are combined in one (1: 1) mixing phase, followed by a balanced split, resulting in the production of two same size droplets

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