Sensors and Actuators A 250 (2016) 15–28

Contents lists available at ScienceDirect

Sensors and Actuators A: Physical

journal homepage: www.elsevier.com/locate/sna

Review

Perspectives on digital microfluidics

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ARTICLE INFO

Article history:
Received 18 December 2015
Received in revised form 31 July 2016
Accepted 14 August 2016
Available online 20 August 2016

Keywords:
Digital microfluidics
Lab-on-a-chip
Electrowetting on dielectric
Dielectrophoresis
Surfaces
Applications

ABSTRACT

Digital microfluidics (DMF) is a technique for manipulation of discrete droplets on a substrate, which allows timed motion of fluids, with accurate control, representing an alternative to steer away from the conventional paradigm of transporting fluids in enclosed channels. This review addresses the techniques for droplet control, starting with the most common, involving forces of electric origin, followed by other methods currently utilized. A discussion of the basic geometries employed, often utilizing AC voltages, is followed by a section discussing current alternatives to reduce the interaction between droplet and surfaces, frequently associated with device failure. Subsequent sections address the interfacing of DMF with other techniques, and current applications, which include topics like immunoassays, nucleic acids, proteins, cells, and studies of multicellular organisms. In addition, the integration with electromechanical systems and semiconductor structures, with still a modest number of applications, can potentially impact the development of new technologies.

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http://dx.doi.org/10.1016/j.sna.2016.08.007

1. Introduction

The miniaturization in liquid handling might be seen as a natural sequence to the sheer progress provided by the developments in solid-state miniaturization. From electronic valves used to fabricate the first computers, to the small transistors that populate electronic chips, it is quite exciting to think that this paradigm can somehow be translated into miniaturizing an entire laboratory for a variety of applications, a lab-on-a-chip (LOC) concept. In this direction, during the last twenty years, techniques and materials from solid-state fabrication (and also new ones, including polymers like polydimethylsiloxane (PDMS) [1]) have been utilized to fabricate microchannels, with a variety of applications, also involving the manipulation of droplets in enclosed channels (see, e.g., Nge et al. [2] and references within for a review).

Here, the focus is on an alternative technique to move discrete droplets on a substrate, named DMF. In its most popular form (several others are included below), motion is achieved by the controlled application of voltages to an array of electrodes, via electrowetting on dielectric (EWOD or EWD) or dielectrophoresis (DEP), with a number of demonstrated applications involving a variety of liquids.

One of the major benefits of DMF is that fluid motion and control is achieved without pumps and valves, and clogging is not an issue. However, interfacing capabilities with other techniques are still under improvement, and, since droplet volumes are in the nano- to microliter range, evaporation can limit operation, particularly in open plate configurations. In addition, the interaction between surface and droplet can hinder motion. This surface fouling, which is dependent on droplet contents, is a major challenge in DMF.

Overall, the development of surfaces with reduced interaction with liquids continues to be subject of intense research, e.g., to reduce drag in pipes [3] and anti-soil textiles [4], among a variety of other applications (see, e.g., [5,6] for a review). Here, the surfaces for applications in DMF are discussed, presenting the current available approaches to reduce the interaction between droplet and surface to minimize biofouling, also including some clever applications that take advantage of this interaction. Of particular interest to reduce biofouling are surfaces that lead to apparent contact angles larger than 150° for water and low surface tension liquids like oils. These surfaces have been termed superamphiphobic [7]; however, other terms have been suggested as more appropriate (see Marmur [8] and discussions by Bellanger et al. [9]). Certainly the adoption of a common name could facilitate the tracking of literature in the field, which is quite extensive. Here, the term superamphiphobic is used throughout the paper.

This review builds upon previous ones in DMF (see, e.g., [10–13] and also [14], with emphasis on point-of-care applications), and offers a critical evaluation of the current technology, aiming at serving as a tool to increase its breadth. In what follows, the techniques for droplet control are presented, including a discussion of the electrical mechanisms of force generation. The geometry of DMF devices is then described, followed by a discussion of surfaces and prevention of biofouling. The techniques which interface with DMF are then discussed, including the coupling to the mass spectrometer (MS). Finally, there is a section dedicated to the applications of DMF.

2. Techniques for droplet control

This section presents a summary of the several approaches currently utilized to generate forces for droplet manipulation. It starts with a discussion of forces of electric origin (EWOD and/or DEP; see, e.g., [15,16]), currently the most popular, with plethora of applications as discussed below. Other promising methods are then presented, including force generation associated with optoelectrowetting [17–19], magnetic fields [20], the thermocapillary effect [21], surface acoustic waves [22,23], and acoustophoresis [24].

2.1. Forces of electric origin

The forces of electric origin in DMF are associated with EWOD and DEP. Before approaching these mechanisms, however, a discussion follows providing an introduction.

To study these forces, the discussion here starts with the work of Jones et al. [25]. These authors constructed an apparatus composed of two electrodes (width W) separated by a distance D, and coated with a dielectric of thickness d, to study the effects of variable, alternating electric fields, on the height of rise h of an aqueous liquid of density ρ (Fig. 1(a)). In order to consider uniform field between plates, W » D, and d « D. The authors modeled the system (Fig. 1(b)) considering the conductivity (σ_L) and capacitance of the liquid (C_L), and the capacitances of air (C_{air}) and dielectric layers (C_d). The air and dielectrics have negligible conductivity. The capacitance of the electric double layer (EDL) is also considered to make a negligible contribution to the total force, considered to be a valid approximation for a variety of electrolyte solutions [11]. The Maxwell stress tensor was then used to obtain the vertically directed forces of electric origin, which could be compared to the experimental results from the measured height of rise of the liquid. The average force $\langle F\rangle$ is then given by:

$$\langle F\rangle = \rho g W D k^* V_{RMS}^2, \tag{1}$$

where g is the acceleration of gravity, V_{RMS} is the root of the mean square of the applied voltage, and k^* is a frequency-dependent coefficient that takes into account all material parameters (see [25] for details). Two limiting cases of particular interest are highlighted below, which are the perfectly insulating, and the perfectly conducting liquid at a given frequency. The average forces are given, respectively, by:

$$\langle F\rangle = \frac{V_{RMS}^2 \varepsilon_0 W (k_L - 1)}{2D}, \tag{2}$$

$$\text{and} \ \langle F\rangle = \frac{W k_d \varepsilon_0 V_{RMS}^2}{4d}, \tag{3}$$

where ε_0 is the vacuum permittivity, k_L and k_d the dielectric constants of the liquid and of the dielectric coating, respectively.

Associated with the model is a critical frequency given by $\omega_c = \frac{2\sigma_L}{\varepsilon_0 (2k_L + \frac{Dk_d}{d})}$. For frequencies well below ω_c, the liquid acts as perfect conductor, and for frequencies well above ω_c, the liquid behaves as a perfect insulator. This frequency dependence is alternatively explained by Nelson et al. [11]. These authors define a charging time of the dielectric-liquid interface ($\tau_{charge,}$ to be compared to $1/\omega_c$, for a qualitative analysis) and compare it with the period of the AC voltage applied ($\tau_{applied}$). If $\tau_{charge} \ll \tau_{applied}$, the boundary between liquid and dielectric will respond to the field assuming a net charge, shielding the liquid from the electric field. This charge leads to a strong electric field close to the contact line, causing the