Sensors and Actuators B 236 (2016) 794–804

Contents lists available at ScienceDirect

Sensors and Actuators B: Chemical

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

Detection and sizing of single droplets flowing in a lab-on-a-chip device by measuring impedance fluctuations

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ARTICLE INFO

Article history:
Received 9 March 2016
Received in revised form 17 May 2016
Accepted 24 May 2016
Available online 7 June 2016

Keywords:
Particle sizing techniques
Two-phase systems
Electrochemical noise
Impedance
Electrolyte resistance
Microfluidic device
Oil droplet

ABSTRACT

This paper is devoted to the evaluation of the electrochemical noise technique consisting in measuring the fluctuations of the electrolyte resistance (ER) between two metallic electrodes immerged in a conductive electrolyte to detect and characterize single particles circulating in a microfluidic device, without the help of optical measurements that require good visibility of the detection region. Numerical simulations were performed with the finite element method to study the influence of the dimensions of the channel and the electrodes on the ER. Measurements of the ER variations due to the passage of oil droplets and plugs passing between the electrodes were carried out. Excellent agreement was obtained between the theoretical and experimental ER transients, which allowed the velocity and diameter of the oil droplets to be estimated with an accuracy of a few percents in the case of droplet diameters ranging from 60 to 100 μm. According to the numerical simulations and the amplitude of the background noise, oil droplets of diameter larger than 20–25 μm can be detected in the microchannel used (cross section of 100 μm × 100 μm and 100 μm × 100 μm electrodes separated by a gap of 100 μm). Developments of smaller microfluidic devices are under progress to detect and characterize particles of a few micrometers, such as biological cells for example.

1. Introduction

Microfluidic systems offer some attractive advantages over standard macroscale techniques for advanced chemistry, material science, biology and medicine since they allow small sample volumes, high sensitivity, reduced analysis time and low fabrication costs [1–5]. These systems, with dimensions typically of tens to hundreds of micrometers, deal with continuous streams of fluids. In contrast, droplet-based microfluidics focuses on creating discrete droplets by mixing two immiscible fluids in a microfluidic channel, at a T-junction or using a flow-focusing technique, in order to enable rapid mixing, no reagent dispersion and high-throughput analysis [6–13]. Indeed, droplets with volumes ranging from femtoliters to nanoliters can be generated at high rates, up to 10,000 droplets per second [14], each droplet serving as an individual microreactor. Applications of droplet-based microfluidics have been demonstrated in the past decade for single-cell analysis [15–17], drug delivery [18,19], and diagnostics [20,21].

Despite many efforts to develop specific devices for droplet generation and manipulation, including droplet moving, merging, mixing, sorting and trapping, the detection and characterization of single droplets remains a challenging task. To date, methods based on optical technologies are the most valuable techniques because of their numerous advantages, such as high sensitivity and fast response [2,14,22–26]. However, optical techniques are often bulky and expensive, and they require a good visibility of the detection volume so that they cannot be used in opaque media. Moreover, the droplets often need to be tagged with fluorescent markers. For these reasons, various non-optical methods have been developed [27,28], among which those using integrated microelectrodes for chronoamperometry [29–32], capacitive [33–35], or resistance measurements [36–42], are particularly interesting since they can be easily integrated with microchips. These techniques have been used to detect biological cells [33,37,38,41,42], water-in-oil or oil-in-water droplets [31,35,39], or to measure the concentration of various species within droplets [30,32,40]. Chronoamperometry consists in measuring the transient increases of the mass-transport limited current due to the passage of droplets in the diffusion layer of the working electrode, which requires the use of a reference electrode and the addition of an electro-active species in the continuous phase or in the droplets. In contrast, impedance spectroscopy is a label-free technique that does not require any reference electrode or electro-active species. Sun and Morgan reviewed in 2010 the different approaches and technologies employed for detecting and

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http://dx.doi.org/10.1016/j.snb.2016.05.123
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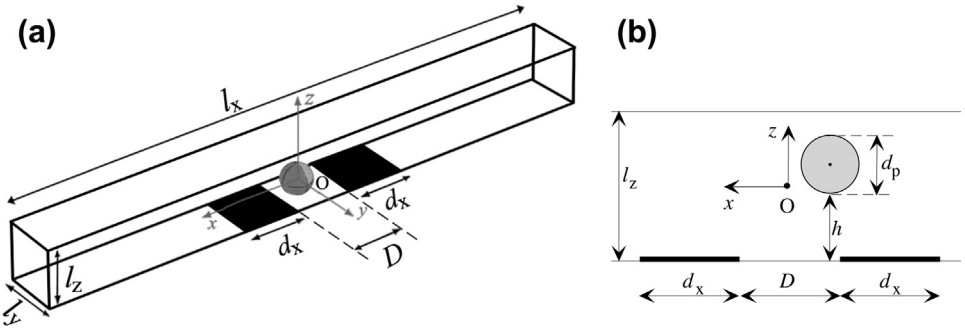

Fig. 1. Geometry of the model. (a) channel and electrodes: l_x, l_y, l_z dimensions of the electrolyte volume, D interelectrode distance, d_x length of the electrodes in the x direction, (b) sphere of diameter d_p and position h above the channel floor.

characterizing single cells with the impedance technique [36]. The impedance is usually measured at a single frequency using two facing or coplanar electrodes [38–40], or three coplanar electrodes [37,41,42], or two pairs of facing electrodes, two of them on the same side of the microchannel being electrically coupled [43,44]. In all cases, the time records of the measured impedance parameter show transients indicating the passage of single cells. However, to the best of our knowledge, non-optical methods capable of precisely measuring a wide range of droplet size in a microchannel have not yet been developed.

Similar developments have been performed in electrochemistry with the electrochemical noise (EN) in two-phase flows consisting in measuring the fluctuations of current, potential or electrolyte resistance (ER) generated by the presence of a solid, liquid or gaseous phase dispersed in a conductive electrolyte. The EN technique is able to provide information on the elementary events at the origin of the fluctuations, such as the position, velocity, trajectory, and residence time of a particle in front of or in contact with a sensor [45,46], the composition of an oil-in-water emulsion [47], the detachment frequency and size of evolving bubbles [48], the activity of pitting corrosion in multiphase flows [49], etc. For particles flowing in a channel, the ER fluctuations give direct information on the changes in electrolyte conductivity due to the passage of particles between the electrodes. The specific technique developed in our laboratory to measure the ER fluctuations between two electrodes [50] has been recently used to detect and characterize single particles of millimetric size flowing between two facing electrodes in a macrochannel [51]. This paper presents the necessary developments of the technique to measure the ER fluctuations and characterize droplets in a microfluidic channel.

2. Theoretical simulations

The model of the microdevice is shown in Fig. 1. The electrolyte of conductivity κ is contained in a cuboid of dimensions l_x, l_y, l_z. Two identical metallic electrodes of dimensions d_x, l_y are mounted flush in the floor of the channel at a distance D between them. Compared to the size of the electrodes ($d_x = l_y = 100\ \mu m$) and the interelectrode distance ($D = 100\ \mu m$) used in the experimental section, the l_x value was large enough (1 mm) to have no significant influence on the simulation results. The centre O of the Cartesian coordinates x, y, z corresponds to the centre of the cuboid. The particle is an insulating sphere of diameter d_p that will flow along the x-axis in the experimental section. Its position is defined by the coordinates x, y, z of its centre. The vertical position z can also be defined as a function of the distance h to the floor of the microchannel below the particle:

$$z = h + d_p/2 - l_z/2 \quad (1)$$

To calculate the ER between the two electrodes in the absence or in the presence of the particle, an electrical model was used, consisting in the application of a potential $\phi_0 = 30$ mV on one electrode while the other was grounded, the ER being calculated from the resulting current on the electrodes. The potential primary distribution, which does not depend on the (electro-)chemical reactions occurring on the electrodes and on mass transport in the solution, was calculated at any point between the two electrodes by integrating Laplace's equation:

$$\nabla^2\phi = 0 \quad (2)$$

where ϕ is the electrical potential in the solution, with the following boundary condition at any point of the insulating surfaces (sphere and boundaries of the cuboid): the normal component of the current is equal to 0 so that the normal component of the potential gradient $\partial\phi/\partial n$ is equal to 0 as well. This was done by using the finite element method with the COMSOL Multiphysics 4.1 software. To improve the accuracy of the simulation results, small mesh elements were used (maximum size of 1 μm on the surfaces of the sphere and the electrodes instead of 55 μm in the volume of the cuboid) and the maximum element growth rate was 1.3.

The distribution of the current density, J, in the cuboid could then be determined according to the following expression:

$$J = -\kappa\nabla\phi \quad (3)$$

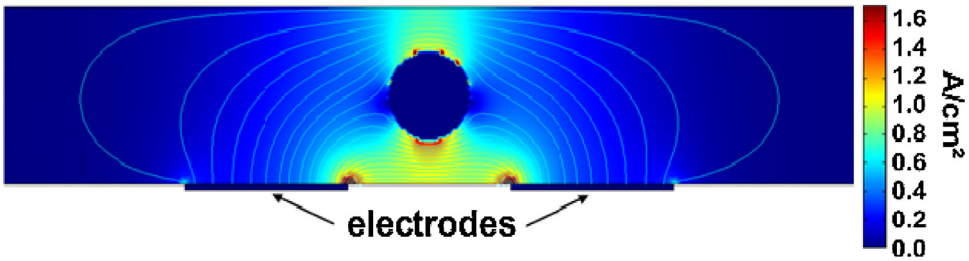

Fig. 2. Distribution of the current lines in the Oxz plane in the presence of an insulating sphere (blue disk) between the two electrodes ($x = y = 0$, $z = 0$, $d_p = 50\ \mu m$, $\kappa = 45.5$ S/m). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)