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Research paper

Manipulation schemes and applications of liquid marbles for micro total analysis systems

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A R T I C L E I N F O

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A B S T R A C T

Micro total analysis systems (microTAS) provide the opportunity to create complete analytical microsystems by integrating various functional modules, such as sample preparation, separation and detection, into a single chip-sized microfabricated device. Microfluidics is the enabling technology for implementing the concept of microTAS. Liquid marble (LM), as a promising separate digital microfluidic platform, has the great potential to enhance the broad applications of microTAS. LMs are small liquid droplets encapsulated by multilayered hydrophobic particles and have attracted a great interest from the microfluidics research community due to their non-wetting property. A LM maintains its integrity and exhibits low friction on various carrier surfaces, enabling the LM to be actuated by external electric, magnetic, gravitational and acoustic fields or other manipulation schemes. LMs can thus serve effectively for the storage and transportation of small liquid volumes. In addition, they have been widely used for the quick detection of water pollution or gas emission and, most importantly, micromixing and microreactions for chemical and biomedical purposes. This paper reviews the recent developments in the manipulation techniques and emerging applications of LMs. The review aims to facilitate better understanding of their use as a unique digital microfluidic platform to promote further advancement of microTAS. The paper begins with different manipulation schemes of LMs according to the nature of actuation energy. Next, it summarizes the diverse applications of LMs for various chemical and biological assays. Finally, this paper concludes with future perspectives regarding the research on LMs in microTAS technologies.

1. Introduction

Starting from a humble gas analysis system and microelectromechanical systems integrated on silicon chips for chemical analysis, the field of micro total analysis systems (microTAS), also called “lab on a chip (LOC)”, has developed rapidly since the establishment of microTAS concept, first proposed by Manz et al. [1]. Currently, microTAS has received much attention from a broad spectrum of scientific and engineering disciplines and has been successfully used for diverse applications in analytical chemistry [2–9] and biology [10–16]. In general, the most important advantage of microTAS is the possibility of creating complete analytical microsystems by integrating various functional modules, such as sample preparation, separation and detection, into a microfabricated device and often reducing the entire laboratory room down to a single chip, Fig. 1.

The enabling technology for implementing the concept of microTAS is microfluidics, which allows for manipulating samples and reagents within small liquid volumes [7]. According to the way how these small amounts of liquid could be handled and manipulated, microfluidics is classified as continuous-flow microfluidics and digital (droplet-based) microfluidics (DMF) [17]. In particular, DMF is an emerging liquid-handling technology dealing with the manipulation of discrete droplets, rather than continuous flows of liquid [18]. In DMF, droplets on the order of microliter serve as miniaturized reaction chambers. This process has numerous advantages such as minimum reagent requirement, fast response rates, low cross-contamination and, more importantly, the capability of performing parallel tests. These advantages make DMF a perfect candidate for practical LOC, microTAS and point-of-care diagnostic devices for clinical use [19–23]. DMF can be further categorized, based on the droplet type, as droplet-based DMF and liquid-marble-based DMF [17, 24].

As an individual digital microfluidic platform, liquid marble (LM) is a rapidly growing research area in microTAS. A LM is a relatively small liquid droplet encapsulated by a porous protective coating that consists of multilayered micro- or nanometer-sized powders. Most coating powders are hydrophobic, which allows a LM to be manipulated like a soft solid [25–31]. The porous protective coating physically isolates the liquid core from its surroundings but allows for the transport of gas or

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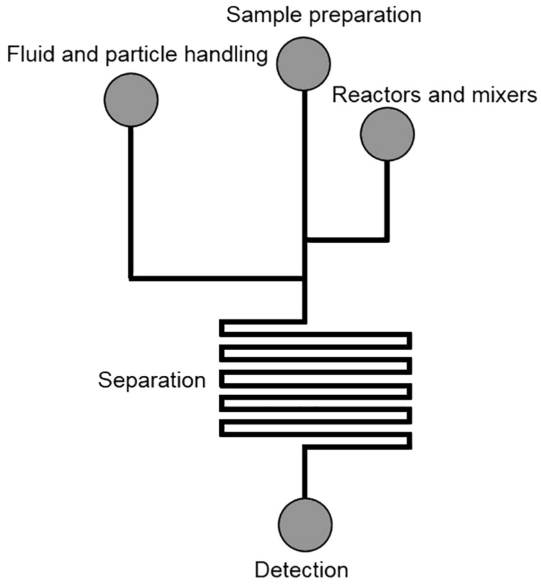

Fig. 1. Schematic of key functional modules that can simultaneously be incorporated into microTAS.

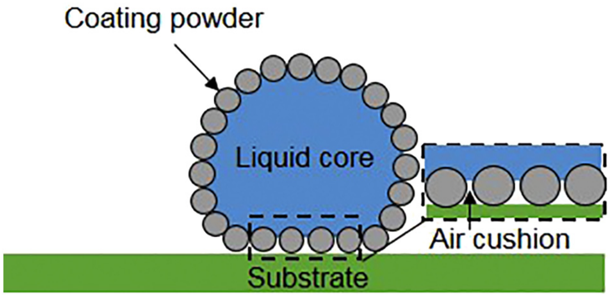

Fig. 2. Schematic of the structure of a LM resting on a substrate.

vapour across the coating layer [24]. Due to the non-stick property enabled by the air cushions between coating particles and the carrier substrate, Fig. 2, LMs exhibit ultra-low friction on various carrier surfaces. This feature allows LMs to move easily across solid and even liquid surfaces without any liquid leakage. Therefore, LMs can be regarded as a promising alternative to superhydrophobic surfaces in the transportation of small amounts of liquid. Compared to bare droplets on a superhydrophobic surface or oil-immersed systems in DMF, LMs have several significant advantages: (i) reduced droplet evaporation rate as compared to bare droplets [32–34]; (ii) lower possibility of cross-contamination and more accessibility of the liquid inside LMs; (iii) no need for complicated fabrication of micro-electrodes as compared to electrowetting-on-dielectric (EWOD); and (iv) low cost and great convenience for rapid production [35].

A LM is formed by simply rolling a liquid droplet over a bed of hydrophobic powder, which may produce a random aggregate of particles, or by other methods, such as the electrostatic formation [36] and dropwise condensation [37]. In the conventional rolling method, the hydrophobic powders assemble on the droplet surface, effectively creating a protective coating. LMs thus can rest stably and roll on a solid substrate or even float and slide on a liquid surface for some time before dissipating via evaporation [38–41]. A large variety of coating materials and liquid cores have been selected to create LMs successfully and the combination of powders and liquids will ultimately determine the properties of LMs and corresponding manipulation schemes. The stability and other performance indexes of different LM compositions have been studied comprehensively by McEleney et al. [42] and Zang et al. [43]. For DMF, samples in LMs can be transported with minimal energy and practically zero cross-contamination. When two LMs are placed into contact, they do not coalesce naturally, even though they are pressed against each other. The pronounced elastic property of LMs enables them to sustain a completely reversible deformation of up to 30% [44–46]. However, LMs can be forced to merge with each other via impact [47–49], which demonstrates the possibility of using LMs as reactors and mixers at the microscale by coalescing two or more LMs containing different reagents or ingredients.

As mentioned above, a LM maintains its integrity and exhibits low friction on various carrier surfaces. This characteristic enables LMs to be actuated in different external fields, such as electric and magnetic fields [50–53], or even to be transported by light-driven motion [54]. In terms of practical applications of LMs, apart from offering controlled liquid manipulation and transportation [27, 55–57], LMs also exhibit a great potential for their use as miniature laboratories in microTAS, where small-scale laboratory operations such as microreactions and detections for analytical chemistry and biotechnology, can be performed [35, 58–60].

Based on the concept of microTAS, this paper reviews recent developments in the manipulation techniques and emerging applications of LMs and aims to facilitate better understanding of their use as a novel digital microfluidic platform to promote further advancement of microTAS. The review begins with different manipulation schemes of LMs according to the nature of actuation energy. A discussion follows on the diverse applications of LMs in microTAS for chemical and biological assays. Finally, this paper concludes with perspectives regarding future research on LMs in microTAS technologies.

2. Manipulation schemes of liquid marbles

The manipulation of LMs enables LM-based digital microfluidic platforms to be implemented in different modules of microTAS such as sample handling, reaction and mixing at the microscale and sample detection. There have been some review papers on the fundamental physics, properties and applications of LMs [27–30] after the first report on the concept of LM by Aussillous and Quere [26]. However, there are few reviews on the manipulation of LMs except for the work of Ooi and Nguyen [25], which systematically classified the manipulation schemes of LMs according to the nature of actuation energy. This review paper further summarizes the manipulation schemes of LMs proposed in recent years based on this classification method, Fig. 3.

2.1. Electric schemes

Electric-field actuation as a means to manipulate a LM is attractive because there is no need for physical contact between electrodes and liquids inside LMs. Besides, accurate control can be easily achieved by varying the applied voltage. However, this scheme also has some drawbacks such as the requirement for high voltage and unavoidable charging of coating particles [25].

2.1.1. Electrostatic force

A number of researchers have demonstrated that an electric field could deform, move or change the wettability of a LM [27, 28, 51, 52, 57, 61, 62]. The electric energy applied to a stationery LM in an electric field causes an increase in surface energy that deforms the marble or an extra increase in kinetic energy that moves the marble. Aussillous and Quere [27] initially reported the presence of electrostatic effect by using a charged Teflon stick to levitate a LM against gravity. They observed a successive bounce of a lycopodium coated water marble between a metal plate and the charged stick. When the charged stick was displaced and kept at a distance to the marble, a motion of the marble was induced.

Bormashenko's group conducted a series of experiments by applying a uniform electric field to LMs [51, 52, 61, 62]. The applied electric field generated an upward electrostatic force that opposed gravity and