Talanta 121 (2014) 163–177

Contents lists available at ScienceDirect

Talanta

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

Review

Microfluidic fabrication of multifunctional particles and their analytical applications

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ARTICLE INFO

Article history:
Received 26 November 2013
Received in revised form
20 December 2013
Accepted 25 December 2013
Available online 7 January 2014

Keywords:
Multifunctional particle
Janus particle
Microfluidic fabrication
Analytical application

ABSTRACT

Multifunctional particles have attracted extensive interest in scientific community in recent years for their capability in combining different functions within a single device. The present review focuses on the preparation methods of multifunctional particles using microfluidic techniques, and the applications of multifunctional particles in analytical and bio-analytical chemistry. As confirmed by most research works, microfluidic fabrication platforms can provide multifunctional particles with precisely controlled structure, high homogeneity and good reproducibility. Meanwhttp://live.elsevierproofcentral.com/authorproofs/macm84f82089f9eab0d214807a46cda8088e/supplier hile, multifunctional particles are proved to have enormous promise when applied in bio/chemical analysis. This paper aims to offer a path for the readers to get acquainted with state-of-the-art progress in these advanced materials from the viewpoint of microfluidics.

Contents

1. Introduction

Multifunctional particles (MPs) have drawn considerable attention of researchers in recent years. Owing to the unique feature of

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http://dx.doi.org/10.1016/j.talanta.2013.12.060

bearing various functions in an integral whole, MPs have more extensive applications than monofunctional particles. As proved by a growing body of researches, MPs perform excellently in catalysis, sensing, biomedicine and display, *etc.* [1–4]. Particles possessing multiple components and properties are what is studied within the scope of MPs, mainly including anisotropic particles among which Janus particles are the most widely investigated, core–shell particles in which the core and the shell act distinct roles, as well as homogeneous particles incorporated or conjugated with other functional species. Notably, structures and functions of MPs can be flexibly adjusted to fulfill the requirements of particular applications, thus MPs are expected to open exciting opportunities in the applied fields where cooperative effect is highly desired.

Bulk production processes of MPs often come across such problems as polydispersity, poor reproducibility and lack of precision in constructing sophisticated structures [4]. The emergence of microfluidic techniques has paved a new way for fabrication of high-quality MPs. High mass and heat transfer rates, accurate control of reaction conditions, fast mixing and low reagent consumption can be achieved in microfluidic platforms [4,5], and these features make microfluidics a powerful tool in preparation of functional particles. Synthesis of MPs in a microfluidic system is greatly beneficial to controllable size and structure, high homogeneity and reproducibility, as well as simplified fabricating processes, *etc.* To the best of our knowledge, there are two major strategies in microfluidic fabrication of MPs: droplet-based method and flow-lithography-based method. The former is competent for producing spherical or sphere-like particles, while the latter is an ideal alternative for designing non-spherical particles, such as rods and flakes, which are more desirable in some particular applications. In short, microfluidics can provide a rather flexible platform for fabrication of MPs.

MPs can be designed to possess optical, electrical, magnetic or other properties that can be utilized for sensing and detecting. In fact, MPs have already shown promise in many analytical approaches. They can act as carriers in high-throughput screening, sensors for sensitive and selective detection, valves to control the fluids in lab-on-a-chip systems, as well as reporters for living cell imaging. The MPs always lead to better outcomes in comparison with monofunctional particles in these applications. The above mentioned are quite far from the entire potential applications of MPs, which could be extended to nearly every branches of analytical chemistry as the MPs can be versatilely designed.

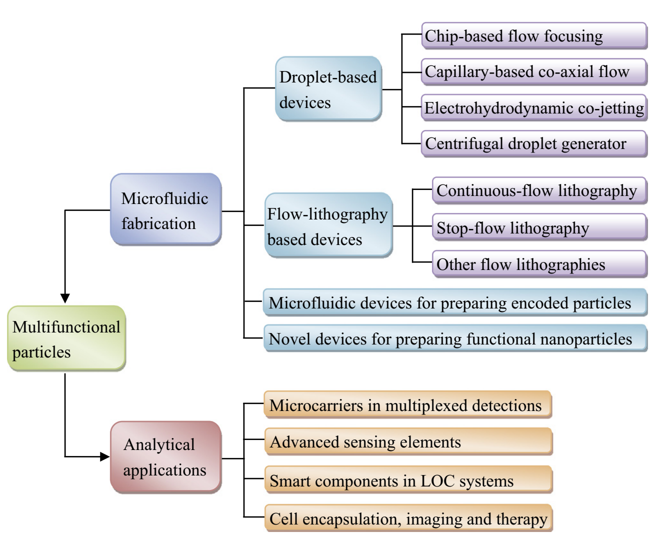

Fig. 1. Schematic diagram of the classification of microfluidic fabrication protocols and the analytical applications of multifunctional particles.

An increasing number of researches are devoted to the preparation and applications of MPs, and also there are some reviews that have summarized these studies from different points of view [1,3,4,6,7]. In this review, we will focus on the microfluidic methods for preparation and applications of MPs both in microscale and nanoscale. Fig. 1 illustrates the general organization of this article. The microfluidic fabrication methods are classified and described in detail, and representative and outstanding work is included while fresh achievements are highlighted. The present review aims to unfold the superiorities of microfluidic methods for MPs preparation and the huge potential that MPs have exhibited in analytical chemistry, which may help the readers to get acquainted with these advanced materials. Meanwhile, possible challenges are also proposed.

2. Microfluidic fabrication devices

2.1. Droplet-based devices

Microfluidic droplets are excellent templates in creating MPs, and several polymerization approaches such as UV exposition, thermal treatment, and ion-induced cross-linking are usually employed to solidify the droplets to obtain MPs. In microfluidic systems, droplets are usually formed by shear force between two immiscible fluids, which are described as dispersed phase (droplets) and continuous phase. So far, the most efficient droplet-based devices for fabricating MPs are chip-based flow focusing device (usually a main channel with two side channels on a chip) and capillary-based co-axial flow focusing device (coaxially aligned microcapillaries). Beyond these methods, other droplet-based strategies with good performances in fabricating MPs, such as electrohydrodynamic co-jetting methods and centrifuge-based droplet formation methods, are summarized as well.

2.1.1. Chip-based flow focusing

Y-shaped channel patterns are typical schemes for generating Janus particles in chip-based flow focusing methods [8,9]. As depicted in Fig. 2A, black and white monomers (carbon black and titanium oxide dispersed into an acrylic monomer respectively) were respectively introduced into the arm channels of the Y junction, and they formed stable biphasic laminar flow in the main channel. The biphasic flow was further sheared into Janus droplets by symmetrically flowing aqueous streams at the orifice. Subsequent off-chip thermal polymerization of these template droplets gave rise to bicolored Janus particles with electrical anisotropy which could be used in color switching display actuated by an electric field [8]. Flow-focusing devices combined with in situ UV-irradiation polymerization could be very efficient for the creation of Janus particles or even ternary particles (tricompartment particles) with sharp interfaces (Fig. 2B) [10]. Immiscible organic monomers M1 and M2 respectively premixed with photoinitiator were supplied to central channels either side by side (to create Janus morph) or with one inserting to the other like a sandwich (to create ternary morph), and then the monomers formed multi-phasic droplets with the help of shear force imposed by the aqueous phase W in the sheath-flow configuration. Thereafter, the droplets were polymerized into particles through UV-irradiation downstream. The fraction of M1 or M2 in a particle could be readily changed by adjusting the flow rate of each monomer.

Janus particles will play a significant role in biomedical applications for their potential synergistic actions in multiplexing, multi-level targeting and combination therapies [4]. However, UV irradiation or thermal treatment usually involved in the flow-focusing-based synthesis may cause harm to the bioactive