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Review article

Utilisation of micro- and nanoscaled materials in microfluidic analytical devices

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ABSTRACT

Microfluidic devices are receiving an increasing attention from scientific community and commercial sphere especially due to their potential to be low-cost, portable and practical handy analytical devices requiring extremely low volumes of samples and producing reduced amount of waste. Recently, nano- and microscaled particles have found wide application in the fabrication of microfluidic devices thanks to their ability to improve analytical performance. This review covers recent papers describing analytical microfluidic devices benefiting from nanoparticles or microbeads. Interesting concepts utilising magnetic properties of such particles were also included. Possible applications of these devices on analysis of real samples were considered and discussed.

Contents

1. Introduction

The continuous increase in global production and implementation of various improvements in legislation regarding the safety and quality of products also brings new challenges into the associated subfields. Neither the proper production process nor quality control would be possible without disposing with an adequate analytical technique. Due to an increasing demand for time and cost effectiveness, there is an opportunity for new technologies to be preferred instead of conventional ones. Such examples, which are the main subject of this review, are analytical devices utilising microfluidic technology. These microfluidic systems are often indicated in the literature as “micro total analysis systems” (μTAS) or “lab-on-a-chip” (LOC) systems [1,2]. Microfluidic devices are receiving a lot of attention both from the scientific community and commercial sphere, respectively, especially due to their ability to be miniaturised and thus to achieve favourable parameters for fabrication and final use.

In recent years, nanoparticles and microparticles have often been introduced within microfluidics. Except for the fact of being a “fashionable” trend in modern scientific literature, there are obvious benefits legitimising their utilisation. Nanoparticles dispose with different (and in many cases with improved) properties compared to flat surfaces or

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macroscaled particles. Moreover, their attractiveness is enhanced by the ability to be further modified or functionalised [3]. Microbeads are also utilised since they similarly allow surface modification, provide good surface-to-volume ratio for chemical binding [4] and applications such as chemical detection, cell encapsulation and drug delivery [5–7].

In this review, we discuss concrete examples of microfluidic devices utilising nanoparticles or microbeads designed for analytical purposes. Papers dealing with the utilisation of microfluidics solely for the synthesis of nanoparticles or microbeads are not included. The selection was predominantly focused on the last 5 years together with a few older papers presenting interesting and related concepts. Moreover, references for reviews focused on sub-topics discussed in detail are provided as well.

2. Microfluidics and microchannels

One of the proposed definitions says that microfluidics is a state-of-the-art technology which handles small volumes of liquids (10^{-9} to 10^{-18} L) being transferred within an area with dimensions of tens to hundreds of micrometres often called microchannels [8]. Thanks to these characteristics, microfluidic devices are suitable candidates for analytical purposes, since small volumes of reagents and samples are used. Also, low fabrication cost, in some cases biocompatibility, the possibility of miniaturisation, reduced volume of waste, easy customisation and transportation are other advantages. Thanks to these properties allowing microchannels to be practical handy devices, microfluidic chips may be applied in clinical diagnostics, especially in point-of-care testing [2,9,10], environment monitoring [11–13], food, agriculture and biosystems industries [14–16] or biochemical kinetic studies [17–19]. Although microchannels have numerous advantages and show a real potential for routine laboratory or in situ applications as illustrated in this review, their success within the commercial sphere is still minimal. Among the most serious reasons is most probably the insufficient verification and proper method validation in case of analyses of real samples and more complex matrices; poor or unverified analytical robustness of the whole system; fact that many devices were designed and tested only for one target analyte or utilising one enzymatic pathway (in case of enzyme-based measuring techniques); the necessity for additional detector and equipment or complicating scaling-up of the manufacturing process may also play a negative role in marketing plans.

Microfluidic devices are conventionally made by etching or moulding microchannels into a working layer and then covered by another layer (Fig. 1). In practice, many microfabrication techniques were originally developed by the semiconductor industry. Silicon micromachining techniques started in the 1950s and have attained a high level of perfection since. Nevertheless, the degree of excellence of silicon micromachining techniques, the requirement of rapid prototyping of different microsystems allied with fact that silicon micromachining is a time consuming and expensive technique, drove the researchers to find new ways to construct microchannels using simpler procedures. Nowadays, the literature shows many alternative approaches for microchannel construction, including micromachining [20], soft lithographic micromoulding [21], hot embossing [22], laser ablation [23] or powder injection moulding [24].

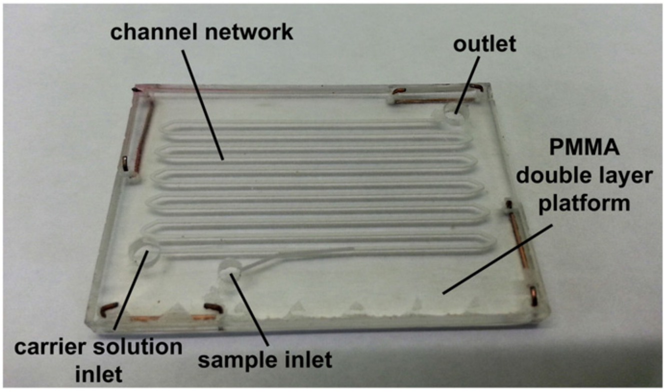

Fig. 1. Example of a microchannel device fabricated from poly(methyl methacrylate) (PMMA) by CO_2 laser engraving.

A newer approach is represented by fabricating a layer with microchannels and integrated electrodes [25]. Microchannel devices made of thermoplastic polymers are less expensive than those made of glass, less adsorptive towards bio-molecules than polydimethylsiloxane (PDMS) and suitable to be mass-produced by hot embossing or injection moulding technologies [26]. Thermoplastic polymers such as polycarbonate (PC) [27,28], poly(methyl methacrylate) (PMMA) [29–31], and polystyrene (PS) [32] are the most commonly used materials. Low glass transition (LGT) polymers, such as PC and PMMA are not suitable for modification by the photolithography process, since high temperatures lead to deformation of the polymer material. However, a novel photolithography process using infrared radiation pre-baking for high precision metal patterning on LGT polymer substrates was recently introduced [33]. A creative method for the construction of microchannels was introduced by do Lago et al. [34] utilising a laser printer. The channel was printed directly on polyester film and the second layer of the same material was hot-pressed on this material. Alternatively, the microchannel was printed on the waxed paper and then the toner was transferred to glass or plexiglass surfaces. A second flat piece of the same material was fixed on the toner ink under heating and pressure [35,36].

Paper-based microchannels are also very popular as they are easy and cheap to prepare and their usage does not necessarily require expensive external devices or complicated arrangements [37–40].

3. Nanomaterials and microbeads

Nanoparticles (NPs) and nanotechnologies provide many benefits for electrochemical detection in biosensors [41–43], microfluidics or capillary electrophoresis [44–46]. Moreover, they can also be valuable for the fabrication of conductive matrices [47–49] or as a platform for enzyme [50,51] or for ligand immobilisation [52]. Large surface areas, chemical inertness and high electrical conductivity are properties that are beneficial for the purposes mentioned above. In particular the high surface area allows analytical characteristics such as lowering detection potential, increasing sensitivity, improving detection limits and stability to be enhanced [46].

There are many strategies that take advantage of nanoparticles in association with microfluidic devices. Magnetic nanoparticles (MNPs) provided an extra degree of flexibility, as their manipulation (e.g. stirring, positioning and recuperation) can easily be performed using a magnet of a magnetic inductor. The immobilisation of enzymes onto NPs is a challenge; as it is essential to preserve their catalytic activity and favourable conformation. The literature reveals many ways of connecting enzymes to different surfaces and MNPs containing immobilised enzymes, for example those containing cellulose [53] or lipase on their surface [54]. In both studies, it was observed that the immobilised enzymes had higher thermal stability and surprisingly superior activity compared with the free enzymes. Immobilised enzymes on MNPs were also utilised for organophosphate pesticide remediation [55]. A mutant form of the enzyme glycerophosphodiesterase was immobilised on the nanoparticles recovered with poly(amido amine) dendrimer using glutaraldehyde as a linking agent. The authors report the long-term stability of enzymes immobilised in this way, demonstrating that more than 95% of the response was retained after 120 days. MNPs functionalised with complexes containing terminals were explored to capture metal ions in solution and carry them to an electrode surface. In this case, the metals were electrodeposited and