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Review

Nanoparticle-based assays in automated flow systems: A review

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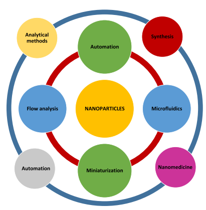
HIGHLIGHTS

- The state of the art of flowing stream systems comprising NPs was reviewed.
- The use of different types of nanoparticles in each flow technique is discussed.
- The most expressive and profitable applications are summarized.
- The main conclusions and future perspectives were compiled in the final section.

GRAPHICAL ABSTRACT



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ABSTRACT

Nanoparticles (NPs) exhibit a number of distinctive and entrancing properties that explain their ever increasing application in analytical chemistry, mainly as chemosensors, signaling tags, catalysts, analytical signal enhancers, reactive species generators, analyte recognition and scavenging/separation entities.

The prospect of associating NPs with automated flow-based analytical is undoubtedly a challenging perspective as it would permit confined, cost-effective and reliable analysis, within a shorter timeframe, while exploiting the features of NPs.

This article aims at examining state-of-the-art on continuous flow analysis and microfluidic approaches involving NPs such as noble metals (gold and silver), magnetic materials, carbon, silica or quantum dots. Emphasis is devoted to NP format, main practical achievements and fields of application. In this context, the functionalization of NPs with distinct chemical species and ligands is debated in what concerns the motivations and strengths of developed approaches. The utilization of NPs to improve detector's performance in electrochemical application is out of the scope of this review.

The works discussed in this review were published in the period of time comprised between the years 2000 and 2013.

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Contents

1. Introduction

Nanotechnology represents one of the most exciting forefront fields for exploitation in analytical chemistry as by means of a wide variety of nanomaterials with distinctive physicochemical properties it could bring about new concepts and trends and provide innovative tools and devices, for facilitating (bio)analytical measurements [1]. According to IUPAC, NPs are particles whose size is comprised between 1 and 100 nm. The broad applicability of NPs is related with their unique and markedly altered physical, chemical and biological properties compared to their macro scaled counterparts [2]. The composition of nanomaterial may include noble metals like gold [3] and silver [2], other metals and metal oxides [4,5], carbon [6], silica, lipid and solid lipid-based particles like liposomes [7], and polymer-based materials [8].

Each type of NP presents assorted and particular physicochemical properties such as high surface-to-volume ratio, surface charge, adjustable solubility, size, shape, variable aggregation tendencies, etc. By designing and controlling the structure of nanoparticles, researchers can influence the resulting properties and, ultimately, modulate materials according to a certain purpose or function.

Fundamental research elucidating NP structure, physical and chemical properties, and toxicity, has led to the development of a large variety of NPs with functional application in areas as dissimilar as electronics, energy, textiles, catalysis, environment, biotechnology and medicine, bio-imaging, bio-sensing, and drug delivery [9–11].

The use of NPs in analytical processes is presently the most extensively exploited area of nanotechnology. This is greatly related with the peculiar properties of NPs that enable the improvement of well-established analytical methods or the development of novel methodologies for new analytes or matrices. Indeed, the emblematic advantages of NPs create conditions to improve the selectivity, sensitivity, rapidity as well as the portability of analytical systems [12].

Regarding their incorporation into particular processes, NPs can be applied in a variety of analytical formats. A typical use is as quantitation tags, when an analyte triggered NP property change (either electrical, optical, thermal, magnetic, chemical) is quantified. In this context, NPs have been applied on the construction of optical (absorbance, luminescence, SERS, SPR), electrochemical, and mass-sensitive sensors [13,14]. In another possibility, NPs can be functionalized to guarantee enhanced applicability since the introduction of modifications of NPs surface usually led to important transformations in their intrinsic physical and/or chemical properties which can confer them novel and specific functions, broadening their suitability for appliance in medical and biological fields [13,15]. In this context, noble metal NPs, in particular AuNPs, and magnetic NPs have assumed great prominence because they could be functionalized with distinct classes of molecules, while assuring high *in vivo* stabilization, thus providing the NPs with the ability to track and to establish interactions with a given biological target. Taking advantage of the abovementioned properties as well as of the comparable dimensions of nanomaterials and biomolecular structures, multiple applications in the referred fields are envisioned. Indeed, the possible uses of NPs in biomedical applications is extremely vast and goes further beyond nanosensing [3,16] as in the case of the utilization of NPs as controlled release reservoirs for targeted delivery of drugs in the treatment of several diseases [17].

Considering the huge potential of NPs utilization, the implementation of NPs-based assays in automated and miniaturized systems will lead to a powerful assembly, particularly when compared to traditional batch-wise procedures. Effectively, in recent years, automated flow analytical methods have widely incorporated NPs for varied applications. Automation of all stages of reaction enables the implementation of effective in-line sample pre-treatments while guaranteeing reproducibility during solutions insertion and reaction zone implementation and transport towards detection. In addition, this strategy provides conditions to carry out the assays in a closed environment, with inherent advantages in terms of reaction control, reactants consumption and analysis time enabling at the same time the implementation of more complex reaction schemes or multiparametric determinations. Furthermore, the easy assembly of flow manifolds through the use of readily-available and low cost equipment and the straightforward coupling to conventional detection systems create conditions for the easy automation of NP based assays by a broad analyst audience without a high level of expertise. On a distinct but not less interesting perspective, flow-based techniques present adequate characteristics for the synthesis of nanomaterials, since they provide large surface areas and reduced diffusion resulting in fast mass transport due to the downsized dimensions of

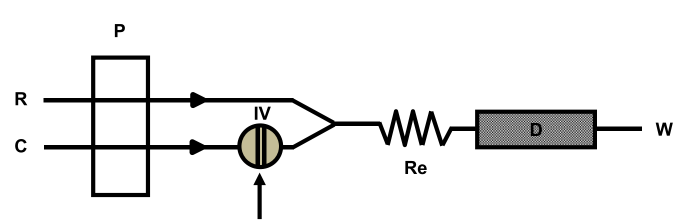

Fig. 1. Schematic illustration of a FIA manifold, where a defined volume of sample (S) is injected by means of a rotary injection valve (IV) into a continuous flowing carrier stream (C) through a pump (P), which is subsequently merged with the reagent (R) stream. After passing a reactor (Re), the ensuing transient generation of product is monitored by a suitable detector (D), and then expelled by the waste (W).