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Review

Analysis of separators for magnetic beads recovery: From large systems to multifunctional microdevices

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ABSTRACT

The use of functionalized magnetic beads has significantly improved the selective separation of compounds from complex fluid solutions compared to conventional technologies. As a result, the capture of non-magnetic compounds through magnetic methods has gained much attention in recent years with current research expanding the concept of magnetic separation to different fields. Nevertheless, the magnetic separation step remains one of the most important stages of these processes and should be carefully analyzed in order to facilitate the successful design of magnetic beads applications. In this work, the fundamental principles of magnetic separations are reviewed in order to establish the underlying theoretical background and to further facilitate the development of efficient magnetic separators. Different alternatives for large scale processes are presented, such as High Gradient Magnetic Separation (HGMS) columns and Open Gradient Magnetic Separation (OGMS) systems, along with their main advantages and practical limitations. Finally, the integration of continuous microfluidic magnetic separators is introduced as a promising alternative for small scale applications due to their multifunctional features.

Contents

1. Introduction

Magnetic nanomaterials have attracted considerable attention in recent years due in part to advances in materials synthesis and a proliferation in applications that leverage the unique properties of such materials. Specifically, nanoscale materials manifest properties that are often different from their bulk state due to the significance of surface and quantum confinement effects among others. These factors affect the chemical reactivity of these materials and their mechanical, optical, electrical and magnetic properties [1,2].

Magnetic nanoparticles exhibit many interesting properties, most notably, superparamagnetism when the size is below certain

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critical dimensions [3]. The critical diameter is material dependent, e.g. 35 nm for Fe_3O_4 [4]. Superparamagnetic nanoparticles provide a strong response to an external field and exhibit very large saturation magnetization values, several orders of magnitude higher than what is observed in paramagnetic materials [5]. Moreover, their magnetic moment vectors relax to random directions (i.e. an unmagnetized state) in the absence of an applied magnetic field in which case, have no attraction for each other, thereby reducing the risk of particle aggregation [3,6,7].

Owing to their unique properties, magnetic nanomaterials (often called "magnetic beads") offer great potential in several fields such as biotechnology, medicine, environmental remediation, imaging, electronics, transportation and telecommunication [1,2,8–14]. However, the focus of most recent research is on their application as magnetic carriers and adsorbents for several biomedical applications such as bioanalysis, medical diagnosis or therapy (drug delivery, cell separation, DNA isolation, bacterial detection, protein purification, enzyme immobilization, blood detoxification, rare cancer cell detection, etc.) [7,8,15–18].

The advantages of employing these materials as magnetic carriers or adsorbents are due to their enhanced properties, i.e. high specific surface area, chemical stability, low intraparticle diffusion rate, high loading capacity, etc. Such properties result to a lower dose and faster kinetics in comparison with conventional materials, thus reducing costs, producing less contamination and improving the selectivity of the process [1,13]. Moreover, their separation from complex solutions is simplified by their superparamagnetic behavior that allows their recovery by magnetic means.

Despite their promising future as adsorbents, the application of magnetic beads in such processes is still limited due to the underlying uncertainty concerning their biotoxicity. Adverse effects on human beings may depend on several factors including their dose, composition, size, structure, route of administration, solubility, surface chemistry, biodegradability, etc. [15]. Therefore, ensuring that magnetic beads can be reliably manipulated with magnetic fields is essential in advancing this novel technology.

The manipulation of these particles under the influence of magnetic fields (magnetophoresis) found its first practical applications in industry during the 1970s [5]. Since its inception, scientists and engineers have been working on the development of efficient designs and the most appropriate magnet arrangements for the separators. Accordingly, numerous types of separators, e.g. continuous or batch, dry or wet, large scale industrial columns or microfluidic devices, etc., have been developed in recent years. Also, there exists a variety of magnetic sources (e.g. permanent magnets (PMs), electromagnets (EMs) or even superconducting magnets (SCMs)) with different designs and material properties that could be selected for each type of separator. Furthermore, the magnet combinations and their position regarding the working volume of the separator are important issues to be addressed in order to generate the appropriate magnetic gradients required for the separation. Thus, there are multiple parameters and operating variables that must be taken into account for the design of the magnetic separation stage.

Although the synthesis and application of magnetic beads as carriers or adsorbents in several fields have been widely studied and reported in the literature, the design and optimization of magnetic separation stages are relatively less studied and rational design is often lacking, especially for microscale separation processes. For example, Fig. 1 illustrates a distribution of the research published in the last 20 years related to magnetic nanoparticles; studies on their separation or other applications. It can be readily observed that although the total number of publications related to the use of magnetic nanoparticles has grown exponentially since the year 2000, only a minority of articles are focused on the subject of magnetic separation. Furthermore, even fewer publications exist on the design and integration of the magnetic separation stage inside the process flowsheet. It can be concluded that more research is required to better understand several aspects related to the optimization of the magnetic separation stage. The development of new materials and their successful applications should accordingly be accompanied by the development of efficient magnetic separation processes. Most importantly, future research should address the process of magnetic recovery of these particles; a crucial stage in the design of magnetic bead-based applications, especially when considering applications in the fields of medicine or water treatment where effective separation is paramount.

In summary, the aim of the current article is to provide an overview of the design of magnetic separators and their applications to recover magnetic beads. We begin with a review of the basic principles of magnetic separations, which establishes the underlying theoretical background and provides useful information regarding the different variables and parameters that must be taken into account for the design of the separation stage. This is followed by an analysis of existing wet, large scale separators with particular focus on the performance of High Gradient Magnetic Separation (HGMS) systems, highlighting advantages and practical limitations for the recovery of submicron magnetic beads. We also introduce Open Gradient Magnetic Separation (OGMS) systems along with their main features. Moreover, the alternatives regarding the magnetic sources that could be employed for large scale processes are also presented. Furthermore, the application of novel microfluidic magnetic systems (MMSs) is also discussed, with an emphasis in the areas of biological or biomedical applications. Within these devices, particle manipulations (separation, trapping, deflection, focusing, etc.) by both positive and negative magnetophoresis are presented. Finally, we describe valuable guidelines regarding the future directions on this field.

2. Fundamentals of magnetic separations

Although humankind has exploited the properties of magnetic materials since the 6th century BC [20], magnetism as a science and its practical application for the separation of magnetic solids

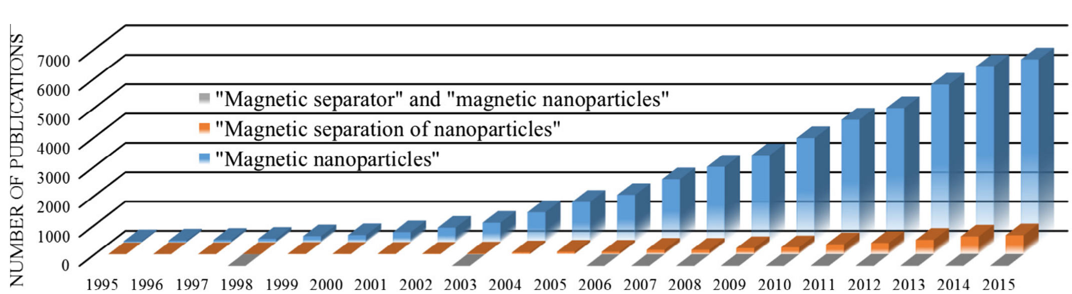

Fig. 1. Number of publications in the last 20 years related to the application and magnetic separation of magnetic nanoparticles [19].