# Centrifugally-driven sample extraction, preconcentration and purification in microfluidic compact discs

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**Centrifugally-driven microfluidic compact discs (μ-CDs) have attracted significant interest within the analytical science community in the past decade, with the primary focus on the potential of such platforms for performing parallel and/or multiplex biological assays and further application in biomedical diagnostics. More recently, μ-CD-based devices were also applied to environmental analysis as platforms for multi-sample extraction and transportation, prior to off-disc analysis in the laboratory. This review critically summarizes recent developments in μ-CD platforms for sample extraction, preconcentration, fractionation and purification in bioanalytical and environmental applications. We also summarize the common methods employed in the fabrication of μ-CD platforms. Further, we discuss preparation of stationary phases in microfluidic channels embedded in μ-CDs, as applications of μ-CDs in sample extraction are generally based on enclosed series of extraction phases and microcolumns.**


*Keywords:* Centrifugally-driven microextraction; Electrophoretic separation; Fractionation; Lab-on-a-disc; Microfluidic compact disc (μ-CD); Monolithic stationary phase; Packed stationary phase; Preconcentration; Purification; Sample extraction

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## 1. Introduction

New trends in the development of analytical instrumentation continue to focus on system miniaturization and automation, in obvious efforts to meet current demands for *in-situ* or on-site analysis, within cutting edge technology areas (e.g., point-of-care diagnostics). Portability, long-term, maintenance-free operation, low-power demand, and integrated sample preparation and analysis are the desired performance characteristics for this type of device.

Microfluidic devices appear to offer a number of advantages in the race to achieve these targets. Indeed, microfluidic platforms have already become well established in many areas of modern science and technology, with their inherent capacity for improved mass and heat transport, speed of analysis, low-volume requirements for sample and reagent, and ability to integrate several analytical operations in a single

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device (e.g., extraction, separation, reaction, incubation and detection). Furthermore, the small dimensions of microfluidic chips facilitate their complete integration into more complete miniaturized, portable instrumentation [1].

Compact disc (CD)-based microfluidic platforms (μ-CDs), also occasionally known as ''lab-on-a-CD'' or ''lab-on-a-disc'' (LOD), present unique features that make them attractive for integration within portable systems [1–4]. Most significantly, the use of centrifugal forces for fluid propulsion presents a clear advantage of μ-CD platforms over other microfluidic devices, as no connections to external pumps or power supplies are needed, and that simplifies enormously the design of the whole system. Parallel sample processing and/or multiplexing analysis is also possible, as many individual structures can typically be replicated radially within a single disc. Also, samples can be reproducibly split into multiple individual chambers by designing microfluidic networks that allow the connection of metering chambers to a supply channel and a waste reservoir, as shown by Lutz et al. [5]. This represents a clear advantage in terms of reproducibility in sample handling, pre-treatment and analysis, as all samples in the disc are processed under the same conditions, as well as in terms of time and costs of analysis. Furthermore, additional forces resulting from spinning the CD can be used to advantage {e.g., Coriolis force can be used to control the direction of the flow at the junction of a channel with two other symmetrical channels [6] or chambers [7]}. Spinning the disc alternately in opposite directions (i.e. clockwise and anti-clockwise) has also been successfully used as a simple, but effective, method for improving the speed of mixing [8,9].

All of the above features have contributed to the growth and the expansion that centrifugally-driven microfluidic devices have experienced in the past 15–20 years within both academic and industrial communities. Several commercial analytical systems based on μ-CD platforms are available from companies (e.g., Abaxis, Gyros AB, Quadraspec, and Samsung). A number of interesting reviews on the topic report the full application history of μ-CD based devices for sample preparation (e.g., sample lysis and plasma separation), nucleic-acid amplification and analysis, immunoassays, DNA-microarray hybridization, cell-based assays and optode-based ion sensors [1–4,10,11].

Among these applications, sample preparation deserves special consideration, as it can be the source of significant error due to sample loss or cross-contamination between samples. A popular application of μ-CD devices in sample preparation has been the separation of plasma from red blood cells in whole blood, which is an essential step in the automation of an immunoassay. Such isolation of target analytes from the sample matrix is often necessary to avoid interferences from other components present in the sample. In many cases, a preconcentration step is also required when dealing with analytes present at very low concentrations, commonly the case in environmental analysis. Those techniques are typically based on the use of a stationary extraction phase (e.g., packed or monolithic microcolumns), upon which the analyte is selectively retained ideally.

The content of this review covers highlights from recent applications of μ-CD to analyte extraction, preconcentration and purification, many of which use on-disc extraction phases of varying dimensions and formats. Also, we discuss work focused on the combination of centrifugal and electrokinetic pumping for sample fractionation. We begin the review with an overview of the most common fabrication techniques employed in the production of μ-CD platforms, together with the preparation of stationary phases within microchannels.

## 2. Fabricating microfluidic discs

A number of established and contemporary methods for the fabrication of microfluidic platforms, both for standard chips and μ-CDs, can be found within the literature. The techniques used for channel formation in μ-CD devices can be divided into seven main categories, namely:

(1) computer numerical control (CNC) milling;
(2) xurography;
(3) laser ablation;
(4) soft lithography;
(5) hot embossing;
(6) injection molding; and,
(7) thermoforming.

Most of these techniques leave open channels, which have to be closed by an additional layer. Closing may be performed by thermal, adhesive, mechanical-based bonding techniques or a combination thereof.

CNC milling is a rapid, relatively inexpensive prototyping technique, widely used in academic research. Several hard polymers have been used in the fabrication of μ-CDs by CNC milling, which demonstrates the utility of this technique, in terms of the substrate.

For example, Puckett et al. fabricated eight replicated microstructures into 3-mm-thick poly(methyl methacrylate) (PMMA), later utilized for simultaneous protein-ligand binding assays [12]. These microstructures comprised several reservoirs connected by channels with different dimensions (635 μm wide and 635 μm deep; and 127 μm wide and 63.5 μm deep), all integrated in a μ-CD of 120 mm OD and center hole of 15 mm diameter. Optically transparent adhesive tape was used to seal the system.

Hoffmann et al. chose cyclic olefin copolymer (COC) as the disc substrate due to its optical properties, low permeability to moisture and temperature resistance [13]. A microchannel network was milled directly into