

ACRYLIC MICROCHANNELS AND THEIR USE IN ELECTROPHORETIC APPLICATIONS

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of application Ser. No. 08/430,134, filed Apr. 26, 1995, now abandoned which application is a continuation of application Ser. No. 08/196,763, filed Feb. 14, 1994, now abandoned, which application is a continuation of application Ser. No. 07/880,187 filed May 7, 1992, now abandoned, which application is a continuation of application Ser. No. 07/487,021 filed Feb. 28, 1990, now U.S. Pat. No. 5,126,022, the disclosures of which are herein incorporated by reference.

INTRODUCTION

1. Field of the Invention

The field of this invention is electrophoresis.

2. Background of the Invention

Electrophoresis has become an indispensable tool of the biotechnology industry, as it is used extensively in the separation, identification and preparation of pure samples of nucleic acids, proteins and carbohydrates. For example, electrophoresis is critical to DNA sequencing applications such as the Maxam-Gilbert and Sanger dideoxy methods, where a major step of these methods is the electrophoretic separation of labeled DNA fragments.

Of increasing interest in the field of electrophoresis is the use of devices having micro cross-sectional dimensions, such as microbore capillaries and microchannels. Use of devices in which the electrophoretic medium is housed in a container having micro cross-sectional dimensions can provide a number of different advantages over conventional slab gel electrophoretic configurations. For example, in capillary electrophoresis (CE) where electrophoresis is carried out in microbore capillaries, one is able to achieve separation and resolution of sample components much quicker than with conventional slab gel configurations. Microchannel electrophoresis (MCE), in which electrophoresis is carried out in micro channels on a planar substrate also provides for shorter run times than is achievable with conventional slab gels. In addition, with microchannels the possibility exists to obtain high throughput applications, where the overall number of samples run per minute is greatly increased. Because much shorter run times are required in CE and MCE, CE and MCE are particularly attractive methods for projects requiring the separation and resolution of complex mixtures of large numbers of differently sized nucleic acids, such as the Human Genome Project.

Traditionally, the material of choice for use in applications such as CE and MCE has been fused silica. Despite the popularity of fused silica as a material for use in electrophoretic applications, fused silica has many shortcomings. The internal surface of a fused silica microchannel, e.g. capillary, under conditions of electrophoresis is negatively charged. This negative charge gives rise to the phenomenon known as electroosmotic flow (EOF) which modulates the flow characteristics of, and therefore affects the separation of, individual sample components in the separation media present in the microvessel. Furthermore, sample components such as proteins and other analytes can adsorb to the negatively charged surface of the fused silica and thereby unpredictably disrupt the uniformity of the EOF, thereby

contributing to the irreproducibility of the results obtained in the electrophoretic application.

To overcome the above problems, various treatments have been developed, including dynamic and covalent modification of the internal surface of fused silica microvessels. See U.S. Pat. No. 5,221,447 for examples of surface modification of fused silica capillaries. Although under ideal circumstances these treatments can reduce or even eliminate the problems associated with EOF and solute adsorption, in practice these treatments can fail to completely mask the negatively charged silica surface. Furthermore, the modified layer on the surface resulting from such treatments may not be entirely stable under the conditions of electrophoresis. Finally, surface modified fused silica microvessels such as capillaries are difficult to manufacture, as the manufacturing process can be laborious and time consuming.

Accordingly, there has been interest in the identification of alternative materials to fused silica from which media containment means, i.e. microchannels, suitable for use in electrophoresis may be fabricated, where good separation and resolution of sample components can be achieved without surface modification of the material. Ideally, such materials would give rise to substantially reduced EOF and/or sample component adsorption as compared with untreated fused silica under electrophoretic conditions. Furthermore, such materials should be moldable, optically transparent for on-line detection, and stable under conditions of electrophoresis.

Relevant Literature

Capillary Electrophoresis is reviewed in Barron & Blanch, *Separation and Purification Methods*, (1995) 24:1-118;

A variety of methods for controlling electroosmotic flow in fused silica capillaries have been reported, including: (1) manipulation of radial electric fields, see Lee et al., *Anal. Chem.* (1990) 62:1550-1552; Lee et al., *Anal. Chem.* (1991) 63:1519-1528; Lee et al., *J. Chromatogr.* (1991) 559:133-140; (2) chemical modification of the fused silica surface, see Belder & Schomburg, *J. High Res. Chromatogr.* (1992) 15:686:693; Vanderhoff et al., *Separation and Purification Meth.* (1977) 6:61-87; Hjertén, *J. Chromatogr.* (1985) 347:191-198; Lux et al., *J. High Res. Chromatogr.* (1990) 13:145-148; and (3) adjustment of electrophoretic medium characteristics, see Lukacs & Jorgenson, *J. High Res. Chromatogr. Comm.* (1985) 8:407-411; Schwer & Kandler, *Anal. Chem.* (1991) 63:1801-1807.

SUMMARY OF THE INVENTION

Microchannels comprising at least an acrylic inner surface and their use in electrophoretic applications are provided. The microchannels of the subject invention have a variety of different configurations and have micro scale inner cross-sectional dimensions. The acrylic inner surface of the subject microchannels gives rise to substantially reduced EOF and/or adsorption under conditions of electrophoresis, as compared to native fused silica, making the subject microchannels particularly suited for use in a number of different electrophoretic applications.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 provides the results of the electrophoretic separation of a 10 base pair DNA ladder in an untreated polymethacrylate capillary and a coated fused silica capillary.

FIG. 2 is a fragmentary cross-sectional view of a device for electrophoretic separation of the present invention.