

FIG. 3B provides a side view of the device of FIG. 3A;

FIG. 4 provides a diagrammatic top view of another embodiment of the subject invention;

FIG. 5 provides a diagrammatic view of an embodiment of the subject invention in which the enrichment channel comprises a single fluid inlet and outlet;

FIG. 6 provides a diagrammatic view of a device according to the subject invention in which the enrichment channel comprises an electrophoretic gel medium instead of the chromatographic material, as shown in FIGS. 1 and 2; and

FIG. 7 provides a diagrammatic top view of disk shaped device according to the subject invention.

DESCRIPTION OF THE SPECIFIC EMBODIMENTS

Integrated electrophoretic microdevices comprising at least an enrichment channel and a main electrophoretic flowpath are provided. The enrichment channel serves to enrich a particular analyte comprising fraction of a liquid sample. The enrichment channel and main electrophoretic flowpath are positioned in the device so that waste fluid from the enrichment channel does not flow through the main electrophoretic channel, but instead flows away from the main electrophoretic flowpath through a discharge outlet. The subject devices may be used in a variety of electrophoretic applications, including clinical assay applications. In further describing the invention, the devices will first be described in general terms followed by a discussion of representative specific embodiments of the subject devices with reference to the figures.

The subject device is an integrated electrophoretic microdevice. By integrated is meant that all of the components of the device, e.g. the enrichment channel, the main electrophoretic flowpath, etc., are present in a single, compact, readily handled unit, such as a chip, disk or the like. As the devices are electrophoretic, they are useful in a wide variety of the applications in which entities, such as molecules, particles, cells and the like are moved through a medium under the influence of an applied electric field. Depending on the nature of the entities, e.g. whether or not they carry an electrical charge, as well as the surface chemistry of the electrophoretic chamber in which the electrophoresis is carried out, the entities may be moved through the medium under the direct influence of the applied electric field or as a result of bulk fluid flow through the pathway resulting from the application of the electric field, e.g. electroosmotic flow (EOF). The microdevices will comprise a microchannel as the main electrophoretic flowpath. By microchannel is meant that the electrophoretic chamber of the main electrophoretic flowpath in which the medium is present is a conduit, e.g. trench or channel, having a cross sectional area which provides for capillary flow through the chamber, where the chamber is present on a planar substrate, as will be described below in greater detail.

Critical to the subject device is an enrichment channel that comprises a sample inlet, a waste fluid outlet, an internal enrichment medium for enriching a particular fraction of a sample, and, optionally, an enriched fraction fluid outlet. The purpose of the enrichment channel is to process the initial sample to enrich for a particular fraction thereof, where the particular fraction being enriched comprises the analyte or analytes of interest. The enrichment channel thus serves to selectively retain and separate the target analyte comprising fraction from the remaining components or the waste portion of the initial sample volume. Depending on the particular application in which the device is employed,

the enrichment channel can provide for a number of different functions. The enrichment channel can serve to place the analyte of interest into a smaller volume than the initial sample volume, i.e. it can serve as an analyte concentrator. Furthermore, it can serve to prevent potentially interfering sample components from entering and flowing through the main electrophoretic flowpath, i.e. it can serve as a sample "clean-up" means. In addition, the enrichment channel may serve as a microreactor for preparative processes on target analyte present in a fluid sample, such as chemical and enzymatic processes, e.g. labeling, protein digestion, and the like.

The enrichment channel may be present in the device in a variety of configurations, depending on the particular enrichment medium housed therein. The internal volume of the channel will usually range from about 1 μ l to 1 μ l, usually from about 1 μ l to 100 nl, where the length of the channel will generally range from about 1 μ m to 1 mm, usually 10 μ m to 1 mm, and the cross-sectional dimensions (e.g. width, height) will range from about 1 μ m to 100 μ m, usually from about 10 μ m to 40 μ m. The cross-sectional shape of the channel may be circular, ellipsoid, square, or other convenient configuration.

A variety of different enrichment mediums may be present in the enrichment channel. Representative enrichment medium or means include those means described in the analyte preconcentration devices disclosed in U.S. Pat. Nos. 5,202,010; 5,246,577 and 5,340,452, as well as Tomlinson et al., supra, the disclosures of which are herein incorporated by reference. Specific enrichment means known in the art which may be adaptable for use in the subject integrated microchannel electrophoretic devices include: those employed in protein preconcentration devices described in Kasicka & Prusik, "Isotachophoretic Electrodesorption of Proteins from an Affinity Adsorbent on a Microscale," *J. Chromatogr.* (1983) 273:1171-28; capillary bundles comprising an affinity adsorbent as described in U.S. Pat. No. 5,202,101 and WO 93/05390; octadecylsilane coated solid phases as described in Cai & El Rassi, "On-Line Preconcentration of Triazine Herbicides with Tandem Octadecyl Capillaries-Capillary Zone Electrophoresis," *J. Liq. Chromatogr.* (1992) 15:1179-1192; solid phases coated with a metal chelating layer as described in Cai & El Rassi, "Selective On-Line Preconcentration of Proteins by Tandem Metal Chelate Capillaries-Capillary Zone Electrophoresis," *J. Liq. Chromatogr.* (1993) 16:2007-2024; reversed-phase HPLC solid packing materials as described in U.S. Pat. No. 5,246,577, Protein G coated solid phases as described in Cole & Kennedy, "Selective Preconcentration for Capillary Zone Electrophoresis Using Protein G Immunoaffinity Capillary Chromatography," *Electrophoresis* (1995) 16:549-556; melttable agarose gels as described in U.S. Pat. No. 5,423,966; affinity adsorbent materials as described in Guzman, "Biomedical Applications of On-Line Preconcentration - Capillary Electrophoresis Using an Analyte Concentrator: Investigation of Design Options," *J. Liq. Chromatogr.* (1995) 18:3751-3568; and solid phase reactor materials as described in U.S. Pat. No. 5,318,680; the disclosures of which are herein incorporated by reference.

One class of enrichment media or materials that may find use as enrichment media are chromatographic media or materials, particularly absorptive phase materials. Such materials include: reverse phase materials, e.g. C8 or C18 compound coated particles; ion-exchange materials; affinity chromatographic materials in which a binding member is covalently bound to an insoluble matrix, where the binding member may be group specific, e.g. a lectin, enzyme