

As mentioned above, capillary electrophoresis systems of the present invention can employ various kinds of detectors. Detection can occur using an ultraviolet, chemiluminescence, refractive index, concentration sensitive, electrical, or conductivity detector. Any detector which can sense a concentration of the desired substance on the column can be used. Thus, the detector to be used is dependent on the molecule to be detected in the capillary electrophoresis system. Appropriate detectors are well known to those of skill in the art.

The double layer thickness (the inverse of Debye length) is a measure of where the electric potential of the inside of the capillary falls off to 63% of maximum. These wall effects are dependent on the chemistry of the system. In systems of the present invention, double layer thicknesses on the order of 0.2 to 10 nm are common.

Control of the electroosmotic flow of a capillary electrophoresis system can also be used in conjunction with pressure for improved bulk flow control. As discussed above, various kinds of control systems for electroosmotic flow can be employed. The method of this invention can be used in conjunction with an electroosmotic flow controller, but control of electroosmotic flow is not needed to apply the method of the present invention. Thus, the use of pressure alone can be used as the bulk flow control method for a capillary electrophoresis system.

However, the advantages of the invention will be realized best when used in conjunction with electroosmotic flow control methods. This is due to the fact that the electroosmotic flow control methods cause an increase in the plate height, and, as FIG. 4 shows for low pH, the addition of pressure driven flow can reduce the plate height. The advantages of the invention are better realized at pH less than 7.0 and best realized when using low pH buffers (less than about pH 4.0), because in a normal capillary electroosmotic system this condition will cause the plate height to rise far about the optimum value (where diffusion is the only factor). In that case, the addition of pressure will improve the plate height, and consequently the resolution. In particular, the addition of downstream pressure, i.e., in the direction of flow, improves plate height under these conditions.

Although the separation capillary has been shown as a single capillary tube, the separation capillary can include more than one capillary column and can have more than one inlet.

In a capillary electrophoresis system according to the present invention, it was discovered that the use of a pressure differential to force flow through a capillary in conjunction with electroosmotic flow unexpectedly results in an average bulk flow velocity with a sharper flow front than is achieved by electroosmotic flow alone under certain conditions. The system of the present invention provides sharp flow fronts while maintaining control over the bulk velocity. Accordingly, it can be appreciated that the above-described invention provides improved control of bulk flow in capillary electrophoresis applications over a broad range of velocities, independent of the chemistry of the system. Moreover, pressure control is independent of voltage and independent of chemistry and is thus an independent way of controlling bulk flow in capillary electrophoretic systems. Thus, pressure control may be useful to reduce the plate height in any situation which perturbs the flow front. However, in practice, a parabolic flow front is formed (laminar flow) if pressure alone is used to force flow in a capillary. This flow front is not as sharp as electroosmotic flow alone, and gives rise to large plate heights.

The foregoing has described the principles, preferred embodiments and modes of operation of the present invention. However, the invention should not be construed as limited to the particular embodiments discussed. Instead, the above-described embodiments should be regarded as illustrative rather than restrictive, and it should be appreciated that variations may be made in those embodiments by workers skilled in the art without departing from the scope of present invention as defined by the following claims.

What is claimed is:

1. A system for controlling the rate of bulk flow in capillary electrophoresis comprising:

- a) a separation capillary having an inlet end and an outlet end;
- b) upstream liquid containment means in fluid flow communication with said inlet end for introducing a solution to said separation capillary;
- c) downstream liquid containment means in fluid flow communication with said outlet end for receiving a flow of said solution;
- d) voltage means for applying voltage between said inlet end and said outlet end;
- e) forward and reverse bulk flow driver effective for selectively driving the bulk flow in both a forward and reverse direction across the length of said capillary through application of differential pressure selectively in a forward and a reverse bulk flow direction across the length of said separation capillary concurrently with the applied voltage;
- f) in which the internal diameter of the capillary ranges from 0.010 to 0.150 mm and the double-layer thickness ranges from 0.2 to 10 nm, such that a ratio between an internal radius of the capillary and a double-layer thickness is at least 500.

2. The system of claim 1 which includes a first and a second pressure means for applying pressure to said inlet end and said outlet end of said separation capillary.

3. The system of claim 1 further including pressure adjustment means for adjusting the pressure differential within said separation capillary.

4. The system of claim 1 wherein said means for applying differential pressure includes means for applying a vacuum.

5. The system of claim 1 further including means for adjusting electroosmotic flow within said separation capillary.

6. The system of claim 1 wherein said solution has pH less than 7.0.

7. The system of claim 1 wherein said solution has pH less than 4.0.

8. The system of claim 1 further including detector means connected to said capillary tube for detecting migration within said capillary tube.

9. A method of controlling the rate of bulk flow of a sample solution in capillary electrophoresis comprising:

- a) providing a capillary electrophoresis apparatus having a flow region between an inlet and an outlet port of a capillary tube, in which the internal diameter of the capillary ranges from 0.010 to 0.150 mm and the double-layer thickness ranges from 0.2 to 10 nm, such that a ratio between an internal radius of the capillary and a double-layer thickness is at least 500;
- b) inducing electroosmotic flow of a solution within said flow region;
- c) applying a pressure differential selectively in a forward and a reverse bulk flow direction across said flow region; and