US005290420A

United States Patent [19]

Matson

[11] Patent Number: 5,290,420

[45] Date of Patent: Mar. 1, 1994

[54] SAMPLING SYSTEM AND ANALYSIS CELL FOR STRIPPING VOLTAMMETRY

[75] Inventor: **Wayne R. Matson**, Ayer, Mass.

[73] Assignee: **ESA, Inc.**, Bedford, Mass.

[21] Appl. No.: **929,702**

[22] Filed: **Aug. 12, 1992**

[51] **Int. Cl.**[5] **G01N 27/26**

[52] **U.S. Cl.** **204/403**; 204/409; 204/412; 204/416; 204/418; 204/419; 204/153.12

[58] **Field of Search** 204/403, 405, 409, 412, 204/416, 418, 419, 433, 434, 435, 413, 153.12

[56] **References Cited**

U.S. PATENT DOCUMENTS

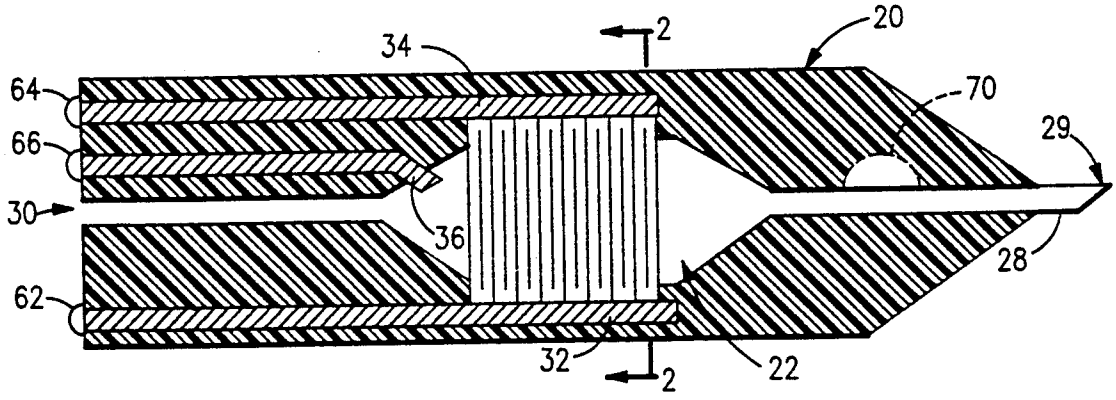
4,090,926	5/1978	Matson	204/413
4,214,968	7/1980	Battaglia et al.	204/418
5,046,496	9/1991	Betts et al.	204/403
5,120,420	6/1992	Nankai et al.	204/403
5,141,868	8/1992	Shanks et al.	204/403

Primary Examiner—John Niebling
Assistant Examiner—Bruce F. Bell
Attorney, Agent, or Firm—Hayes, Soloway, Hennessey & Hage

[57] **ABSTRACT**

A combination sampling/electrochemical analysis cell comprises an enclosure having a hollow therein, at least one inlet leading to the hollow, a vent leading from the hollow, at least one testing electrode, at least one counter electrode, and at least one reference electrode, all disposed at least in part in the hollow. A testing reagent is also contained in the hollow.

29 Claims, 3 Drawing Sheets



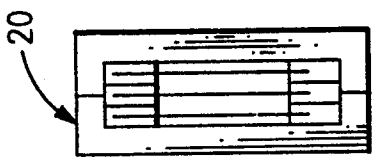


FIG.2

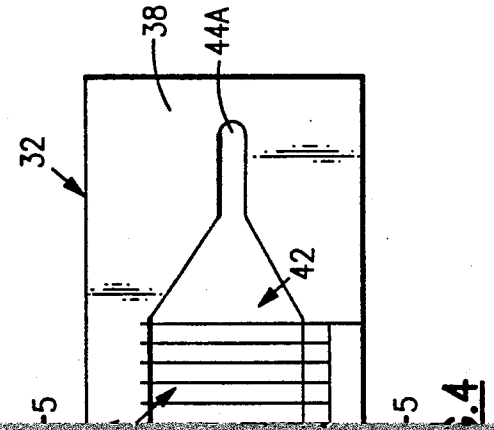


FIG.4

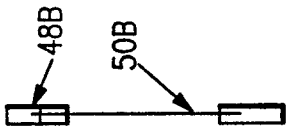


FIG.7

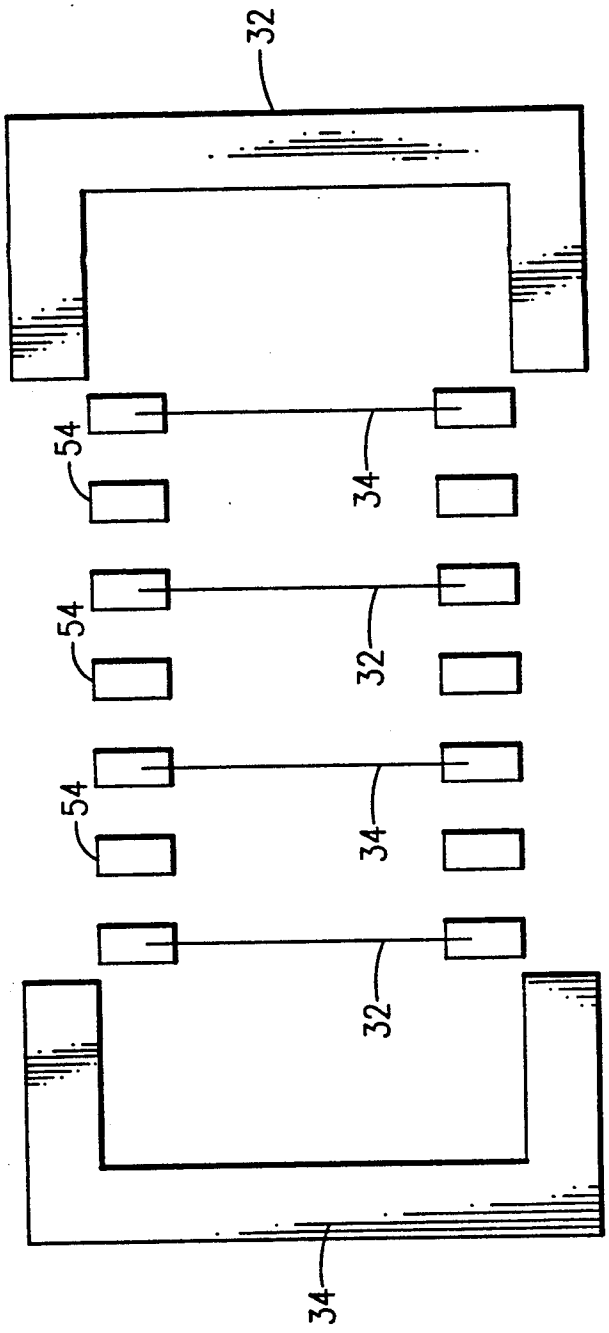


FIG.8

SAMPLING SYSTEM AND ANALYSIS CELL FOR STRIPPING VOLTAMMETRY

BACKGROUND OF THE INVENTION

The present invention relates to electrochemical analysis, and more particularly to an integrated sampling system incorporating electrochemical sensors and reagents. The invention has particular utility in connection with testing lead levels in human blood and will be described in connection with such utility, although other utilities are contemplated.

It has long been possible to test both qualitatively and quantitatively for ionic materials in an aqueous sample by electrolytic means, and to record the electrical potential of deposition of the ions on an electrode. In one form of such testing known as stripping voltammetry, the ions are first deposited on an electrode and thereafter the potential is varied to strip the deposited material from the electrode and redissolve it in the sample liquid. This operation is known as stripping voltammetry and since it is ordinarily used by plating cathodically and stripping anodically to detect and measure metallic ions, it is often known as anodic stripping voltammetry. By means of anodic stripping voltammetry, it has been found possible to perform relatively quickly simple and accurate tests to measure minute traces of materials, for example, to test for the presence of informative or dangerous impurities in the human bloodstream. As a result anodic stripping voltammetry systems such as available from ESA, Inc., the assignee of the subject application, have achieved widespread field and laboratory use since at least about 1975.

The application of stripping voltammetry to testing for impurities in the human blood stream, improved electrochemical detection systems, cells, reagents and processes are the subject of several of my prior U.S. Patents, including U.S. Pat. Nos. 3,855,099, 4,201,646, 4,090,926, 4,374,041 and 4,233,031, and U.S. Reissue Pat. No. 32,920, the disclosures of which are incorporated by reference.

While anodic stripping voltammetry systems provide satisfactory results for the general population, recent studies have shown problems of individual variability affecting low blood level value (5 μg %) accuracy on commercial exchange reagents/anodic stripping voltammetry systems.

Lead in a whole blood sample is distributed in a number of different compartments with a high degree of individual variable in binding constants and kinetics. Similarly, individual variability in copper levels and other endogenous oxidizable/reducible compounds can affect the envelope of the electroanalytical curve and hence the analytical value for lead.

Simplistically, generally 97–99% of lead is bound to the erythrocyte. However, within the erythrocyte there appear to be compartments both on the external surface of the cells and within the cell and sites with varying levels of binding constants. Thus, there is a level of lead typically between 2–10 μg % that will not release into EDTA; a level (typically 2–8 μg %) that will not release into acid; and a level (typically 0.2–2 μg %) that will not release into commercial exchange reagents such as Metexchange ® available from ESA, Inc. The reasons for the variability across a range of individuals is not clear, although in the specific disorder, sickle cell trait, it has been suggested that sickle cells are resistant to rupture and release and that in other cases a high concentration of Fetal Hemoglobin may imply a higher binding constant.

When lead is released from the erythrocyte to a solution matrix of whole blood residue and exchange reagents, it is bound secondarily in a number of labile ligands (sulfhydryls, phospholipids, amino acids, peptides) which in the aggregate change its apparent diffusion constant from 6.9×10^{-6} cm²/sec to approximately 7.8×10^{-6} cm²/sec in a 30:1 dilution to approximately 8×10^{-7} cm²/sec in whole blood with added solid exchanger.

The analytical implications of these observations are that any technique employing direct blood measurement, such as electrochemistry or enzyme coupling, must be designed to handle the extremes of individual variability, and that it is relatively easy to be fooled into assuming technical adequacy by evaluating a technique on pools or artificially spiked samples.

The approach taken in commercial reagent/anodic stripping voltammetry to addressing the problems of lead distribution has been to dilute the blood sample, for example, by 30 times, and to provide the strongest exchange reagent possible consistent with long term sensor operation, and to operate the sensor at 1.5–1.7 half times (1 minute) to significantly reduce the lead level in solution and thus compensate for differing ligand formation constants. Essentially, the approach is a compromise among sensor longevity, sensitivity, accuracy and analysis time.

Other problems in the prior art include sample contamination, for example, due to smearing during blood drawing and sample mislabeling or mixup.

OBJECT OF THE INVENTION

It is therefore an object of the present invention to provide an improved electrochemical analytical system which overcomes the aforesaid and other problems of the prior art. A more specific object of the present invention is to provide an electrochemical analytical system which permits the incorporation of more aggressive exchange reagents without reducing sensor life. Yet another object of the present invention is to provide an electrochemical detection system which permits assay of blood without dilution.

Other objects of the invention will in part appear obvious and will in part appear hereinafter. The invention accordingly comprises the apparatus possessing the construction, combination of elements and arrangement of parts, the process comprising the several steps in relation of one or more steps with respect to the others, and the compositions comprising the several materials, all of which will be exemplified in the following detailed description and scope of application as will be indicated in the claims.

BRIEF DESCRIPTION OF THE PRESENT INVENTION

The present invention provides a disposable integrated sampling/electrochemical analysis cell incorporating one or more testing electrodes and selected exchange reagents directly in the cell. In a presently preferred embodiment of the invention, the cell comprises a capillary inlet to a hollow containing one or a plurality of testing and counter electrodes, and at least one reference electrode. An electrochemical reagent selected for the particular electrochemical test, in dry or high viscosity form is deposited in the hollow, prefera-