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Title: SOLGEL ELECTRODE FOR DETECTING BODY ANALYTES

![Fig. 1](image-url)

Abstract: The present invention provides a hybrid solgel modified electrode. It is an enzyme-enzymatic biosensor that targets biomolecules present in body fluids. The electrode comprises a base substrate [20] in the form of a bowl and a screen printed conductor [22] layer in the substrate. A hybrid solgel composite [24] is layered to cover the conductor [22] and substrate [20] layer, which is sensitive to body analytes by selective voltammetric oxidation of the biomolecules. The hybrid solgel composite layer comprises tetraethyloxysilicate (TEOS), methyltriethoxysilane, phenyltriethoxysilane, carbon material, and ferrocene compounds [26, 28]. A method to fabricate the composite layer is also described. The typical analytes considered among the most important for medical diagnosis by analysis of blood, urine and sweat includes glucose, cholesterol, uric acid, creatine, urea and lactate. This electrode can be used in routine medical screening for both sick and healthy people.
SOLGEL ELECTRODE FOR DETECTING BODY ANALYTES

The present invention relates to hybrid solgel modified electrode for use in bio-medical analysis.

BACKGROUND ART

Bio-medical analysis involves the detection of metabolites level in bodily fluid to diagnose diseases such as diabetes, renal failure and cardiovascular problems. To detect levels of these analytes in blood and urine, enzyme electrodes have been widely employed.

Although the use of enzyme electrode has the advantages of high selectivity nature of enzymatic reaction, the use of enzyme electrode has several disadvantages. The enzymes are proteins and specificity of enzymatic transformation depends on complex three-dimensional interaction between amino acid units in the enzyme. These interactions give secondary and tertiary structures of the enzyme which changes outside living cells. Consequently, enzymatic reactions deteriorate over time while giving inaccurate biosensor data.

Also, enzymes contain numerous reactive sites that may be disrupted during immobilisation step. Furthermore, enzymes are usually stored under chilled conditions which have serious limitation in deployment of mass-produced biosensors. Enzyme denaturing also seriously limits the sensor lifetime.

Due to these reasons, innovation has been made on the bio-medical analysis electrodes. At present, a prior art listed a voltammetric system for assaying biological analytes. It uses conventional enzyme method with redox-couple mediator. Glucose dehydrogenase gives selectivity towards glucose substrate and the calibration and measurement is done by cyclic voltammetry.

Another prior art listed a voltammetric ion selective biosensor which includes a method to detect ionic species in fluids, whereby the selectivity is achieved using coated
conductive solid such as tetrahiafulvalene and detection is done using voltammetric method.

The present invention is made in view of the need to address the disadvantages of using enzyme electrodes while the ion selective sensors only detect ionic species while retaining voltammetric analytical method.

SUMMARY OF INVENTION

The present invention proposes a hybrid solgel modified electrode, non-enzymatic biosensors that target bio-molecules present in body fluids which includes glucose, cholesterol, uric acid, creatine, urea and lactate. The hybrid solgel modified electrode works based on voltammetry method. The electrode comprises a base substrate [20] in the form of a bowl; a screen printed conductor [22] layer in the substrate; characterized by, a hybrid solgel composite [24] layer to cover the conductor [22] and substrate layer, which is sensitive to body analytes by selective voltammetric oxidation of the bio-molecules. The hybrid solgel composite layer comprises tetraethylorthosilicate (TEOS), methyltriethoxysilane, phenyltriethoxysilane, carbon material, and ferrocene compounds [26, 28]. A method to fabricate the composite layer is also described.

BRIEF DESCRIPTION OF DRAWINGS

Fig. 1 is a sectional drawing of the hybrid solgel modified electrode.
Fig. 2 is a drawing showing the structure of ferrocene and ferrocene derivative.

DESCRIPTION OF EMBODIMENTS

Hereinafter, the present invention is described in detail.

The invention involves a hybrid solgel modified electrode for detection of analytes in bodily fluid. The sectional drawing of the hybrid solgel modified electrode is shown in Fig. 1.
The hybrid solgel modified electrode comprises a substrate [20] layer, a conductor [24] layer and a hybrid solgel composite [26] layer. The substrate [20] layer, in the form of a bowl, is to provide mechanical strength to the electrode structure and also to give a good adhesion to the screen printed on the conductor layer. The conductor [22] layer is a screen printed conducting layer to provide electrical contact between the hybrid solgel modified electrode and the readout circuitry. The hybrid solgel composite [24] layer, to cover conductor and substrate, is to detect body analytes by selective voltammetric oxidation of the bio-molecules.

In a preferred embodiment, the process of fabricating the electrode starts with the substrate [20] base of polymeric material such as FR4 with a typical thickness of 0.5mm, being screen printed on the top with a conductive [24] layer, made of silver paste to form a circular shaped electrode of typically 4mm and wire traces. This conductive paint is then cured in the oven at 120°C for 20 to 60 minutes. Insulating paste such as solder mask is then printed to cover the wire traces and to expose the electrode window.

As for the hybrid solgel composite [26], a preferred embodiment of the composite is prepared with an equal ratio of tetraethylorthosilicate (TEOS), methyltriethoxysilane and phenyltriethoxysilane, mixed with 0.1M of hydrochloric acid in deionized water. The mixture is stirred at room temperature for 4 hours. After that, a carbon material; graphite of 10 weight percent (10 wt%) and ferrocene [26] or ferrocene derivative [28] (1 wt%) are added to the mixture and the resulting composition sonicated for 1 minute. The sonicated composition is then aged for 20 hours or at least 1 hour in capped vial. Usually, the hybrid solgel composite layer comprises the following by-weight ratio: 20% to 40% tetraethylorthosilicate (TEOS); 20% to 40% methyltriethoxysilane; 20% to 40% phenyltriethoxysilane; 10% to 35% carbon material; and 1% to 10% of ferrocene compound.

The structure of ferrocene [26] and ferrocene derivative [28] is shown in Fig. 2. The derivative ferrocene must have at least one substitution at the cyclopentadienyl carbon atom. The carbon material that can be used as one or in combination includes graphite, glassy carbon, carbon nanotubes or diamond.
The aged hybrid solgel precursor is then pipetted or dispensed onto the screen printed conductor [22] and substrate layer. The pipetted composition is cured in the oven at 80 °C to 100°C for at least 5 minutes or left at room temperature for at least 1 hour. By then, the hybrid solgel modified electrode is completed. This particular solgel electrode is suitable to be used as a glucose sensor.

Accordingly, the invention disclosed a hybrid solgel modified electrode comprising a substrate [20] layer, a conductor [24] layer and a hybrid solgel composite [26] layer. The hybrid solgel composite is a mixture of tetraethylorthosilicate (TEOS), methyltriethoxysilane and phenyltriethoxysilane, mixed with 0.1M of hydrochloric acid in deionized water, which is then added with a carbon material and ferrocene [26] or ferrocene derivative. The hybrid solgel modified electrode, which is a non-enzymatic biosensors could then be used to detect analytes based on voltammetry method for biomedical analyses.
CLAIMS

1. A solgel electrode for detecting body analytes, comprising:
   a base substrate [20] in the form of a bowl;
   a screen printed conductor [22] layer in the substrate;
   characterized by,
   a hybrid solgel composite [24] layer to cover the conductor [22] and substrate, which is sensitive to body analytes by selective voltammetric oxidation of the biomolecules.

2. An electrode according to claim 1, wherein the hybrid solgel composite layer comprises tetraethylorthosilicate (TEOS), methyltriethoxysilane, phenyltriethoxysilane, carbon material, and ferrocene compounds [26, 28].

3. An electrode according to claim 2, wherein the hybrid solgel composite layer comprises the following by-weight ratio:
   20% to 40% tetraethylorthosilicate (TEOS);
   20% to 40% methyltriethoxysilane;
   20% to 40% phenyltriethoxysilane;
   10% to 35% carbon material; and
   1% to 10% of ferrocene compound.

4. An electrode according to claim 2, wherein the carbon material is graphite, glassy carbon, carbon nanotubes or diamond.

5. An electrode according to claim 2, wherein the ferrocene compounds [26, 28] has at least one substitution at cyclopentadienyl carbon atom.

6. A method of fabricating solgel electrode comprising:
   mixing tetraethylorthosilicate, methyltriethoxysilane and phenyltriethoxysilane with acid hydrochloric in deionized water;
   stirring mixture vigorously in room temperature;
   adding carbon material and ferrocene compound; and
   aging the composite for at least an hour to 20 hours.
7. A method according to claim 6, further comprising:
   - screen printing a substrate [20] layer with a silver paste of conductive;
   - forming conductive [22] layer of circular shaped electrode and wire traces;
   - curing the conductive paint in an oven;
   - printing insulating paste on the conductor [22] layer;
   - dispensing hybrid solgel composite [24] onto the conductor [22] and substrate layer; and
   - curing the composition for in an oven or leaving it at room temperature.
INTERNATIONAL SEARCH REPORT

International application No.
PCT/MY20 1/0001 0

A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl.


According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database consulted during the international search (name of database and, where practicable, search terms used)

EPDOC, WPI & INSPEC: (or electrode?, bio_anode?, bio_cathode?, bio_sensor?, bio_electrode?, G01N 27/327/ic/ec/ecno, SPCE): (or sol_gel, tetraethyl_orthosilicate?, teos, methyl_triethoxysilane?, phenyl_triethoxysilane?, ptes, mtes); (or cup, circular, square, bowl, rectangular); screen_print+; composite; hybrid and similar terms

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
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<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<tr>
<td>Y</td>
<td>WO 1999/022227  A2 (GUO et. al.) 6 May 1999 Refer to the whole document and in particular to abstract and pg 9 section titled &quot;Preparation of Sol-Gel Graphite Mixtures&quot;</td>
<td>1-5</td>
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<tr>
<td>Y</td>
<td>US 5403462  A (LEV et. al.) 4 April 1995 Refer to the whole document and in particular to abstract, col. 3, lines 17-26; col. 7, line 14-22</td>
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[X] Further documents are listed in the continuation of Box C  [X] See patent family annex

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  "A" document defining the general state of the art which is not considered to be of particular relevance
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Date of the actual completion of the international search
29 August 2011

Date of mailing of the international search report
05.09.2011

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Form PCT/ISA/210 (second sheet) (July 2009)
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<td>WO 2010/02 1536 A2 (MIMOS BERHAD) 25 February 2010</td>
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<td>US 63876 14 B1 (CHENG et. al.) 14 May 2002</td>
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This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

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Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.

END OF ANNEX