sensor to the enzyme molecules that are immobilized in the enzyme layer. WO 2007/147475 discloses a diffusion barrier made from a polymer having a zwitterionic structure.

WO 2012/019083 discloses a diffusion limiting membrane comprising a polyurethane, a siloxane and a hydrogel. The membrane is prepared by first mixing the polymers, then depositing the polymers onto the sensor and subsequently evaporating the solvent.

The sensors disclosed in the prior art have only limited long-term stability, especially in in vivo applications.

Problem to be solved

It is therefore an objective of the present invention to provide improved means and methods for forming membranes on an analyte sensor avoiding at least in part the drawbacks of the prior art, in particular with regard to long-term stability and membrane performance.

Summary

This problem is solved by the process for forming a membrane on an analyte sensor as well as the analyte sensor obtainable by this process and by the process for forming a sensing layer on an electrode of an analyte sensor and by an analyte sensor comprising the sensing layer obtainable by the inventive process and the membrane obtainable by the inventive process. Preferred examples of the disclosure which may be realized in an isolated way or in an arbitrary combination are disclosed in the dependent claims and throughout the application.

In one aspect, the present disclosure provides a process for forming a membrane on an analyte sensor, the process comprising the steps:

a) providing the analyte sensor, wherein the analyte sensor comprises at least one substrate and comprises at least one first electrode,

b) providing a polymer solution which comprises components

(A) at least one first polymer which comprises at least one first cross-linkable group, wherein the at least one first polymer is a hydrophobic polymer,

(B) at least one second polymer which comprises at least one second cross-linkable group, wherein the at least one second polymer is a hydrophilic polymer, and

(C) at least one first solvent,

c) contacting the analyte sensor provided in step a) with the polymer solution provided in step b) to obtain an analyte sensor which is coated with the polymer solution,

d) drying the analyte sensor obtained in step c) to obtain a dried analyte sensor which is coated with a polymer blend which comprises the at least one first polymer and the at least one second polymer,

e) curing the polymer blend which coats the dried analyte sensor obtained in step d) whereby the at least one first polymer and the at least one second polymer are crosslinked to form the membrane on the analyte sensor,

wherein the at least one first cross-linkable group and the at least one second cross-linkable group are independently of one another selected from the group consisting of benzophenone groups, azide groups, anthrachinone groups, and psoralen, and wherein the at least one second polymer is different from the at least one first polymer.

In another aspect, the present disclosure provides a process for forming a sensing layer on a first electrode of an analyte sensor, the method comprising the steps:

i) providing an analyte sensor comprising at least one first electrode wherein the at least one first electrode comprises a first electrode material,

ii) reacting the at least one first electrode of the analyte sensor provided in step i) with a functionalizing compound which comprises at least one first group which is reactive towards the first electrode material and at least one second group which is cross-linkable, to obtain at least one functionalized first electrode,

iii) providing a polymer mixture comprising components

(D) at least one mediator polymer which comprises at least one cross-linkable group,

(E) at least one second solvent,

iv) contacting the at least one functionalized first electrode obtained in step ii) with the polymer mixture provided in step iii) to obtain at least one coated functionalized first electrode,

v) drying the at least one coated functionalized first electrode obtained in step iv) to obtain at least one dried coated first electrode which is coated with the at least one mediator polymer,

vi) curing the at least one dried coated first electrode whereby the at least one second group of the functionalizing compound and the at least one cross-linkable group of the at least one mediator polymer are crosslinked to form the sensing layer on the first electrode of the analyte sensor,

wherein in a first step the sensing layer is formed on the electrode of the analyte sensor and in a second step a membrane is formed according to the process of any one of claims 1 to 5 on the analyte sensor comprising the sensing layer on the electrode.

As used in the following, the terms “have”, “comprise”, or “include” or any arbitrary grammatical variations thereof are used in an exclusive way. Thus, these terms may both refer to a situation in which, besides the feature introduced by these terms, no further features are present in the entity described in this context and to a situation in which one or more further features are present. As an example, the expressions “A has B”, “A comprises B” and “A includes B” may both refer to a situation in which, besides B, no other element is present in A (i. e. a situation in which A solely and exclusively consists of B) and to a situation in which, besides B, one or more further elements are present in entity A, such as element C, elements C and D or even further elements.

Further, it should be noted that the terms “at least one”, “one or more” or similar expressions indicating that a feature or element may be present once or more than once typically will be used only once when

introducing the respective feature or element. In the following, in most cases, when referring to the respective feature or element, the expressions “at least one” or “one or more” will not be repeated, notwithstanding the fact that the respective feature or element may be present once or more than once.

Further, as used in the following, the terms “preferably”, “more preferably”, “particularly”, “more particularly”, “specifically”, “more specifically” or similar terms are used in conjunction with optional features, without restricting alternative possibilities. Thus, features introduced by these terms are optional features and are not intended to restrict the scope of the claims in any way. The invention may, as the skilled person will recognize, be performed by using alternative features. Similarly, features introduced by “in an embodiment of the invention” or similar expressions are intended to be optional features, without any restrictions regarding alternative embodiments of the invention, without any restrictions regarding the scope of the invention and without any restrictions regarding the possibility of combining the features introduced in such way with the optional or nonfunctional features of the invention.

In the present disclosure, there is provided a process for forming a membrane on an analyte sensor is disclosed, the process comprising the steps

a) providing the analyte sensor,

b) providing a polymer solution which comprises components

   (A) at least one first polymer which comprises at least one first cross-linkable group,

   (B) at least one second polymer which comprises at least one second cross-linkable group and

   (C) at least one first solvent,

c) contacting the analyte sensor provided in step a) with the polymer solution, provided in step b) to obtain an analyte sensor which is coated with the polymer solution,

d) drying the analyte sensor obtained in step c) to obtain the dried analyte sensor which is coated with a polymer blend which comprises the at least one first polymer and the at least one second polymer,

e) curing the polymer blend which coats the dried analyte sensor obtained in step d) whereby the at least one first polymer and the at least one second polymer are cross-linked to form the membrane on the analyte sensor.

Herein, the indicated steps may, preferably, be performed in the given order, thereby commencing with process step a) and finishing with process step e), wherein, however any or all of the indicated steps, in particular process steps a) and b), may be performed at least partially concurrently and/or step b) may

The inventive process is particularly advantageous as it allows an easy manufacturing of a membrane on an analyte sensor. Preferably, the analyte sensor is coated with the membrane. Additionally, the properties of the membrane can be easily tailored based on the at least one first polymer and the at least one second polymer. The obtained membrane is well defined and has a long-term stable structure. In particular, if the membrane is also covalently immobilized on the sensor surface the durability of the analyte sensor for in vivo applications is particularly improved. Also, the properties of the obtained membrane are easier to predict.

In the present disclosure, there is provided a process for forming a sensing layer on a first electrode of an analyte sensor is disclosed, the method comprises the steps:

i) providing an analyte sensor comprising at least one first electrode, wherein the first electrode comprises a first electrode material,

ii) reacting the at least one first electrode of the analyte sensor provided in step i) with a functionalizing compound which comprises at least one first group which is reactive towards the first electrode material and at least one second group which is cross-linkable, to obtain at least one functionalized first electrode,

iii) providing a polymer mixture comprising

(D) at least one mediator polymer which comprises at least one cross-linkable group,

(E) is at least one second solvent,

iv) contacting the at least one functionalized first electrode obtained in step ii) with the polymer mixture provided in step iii) to obtain at least one coated functionalized first electrode,

v) drying the at least one coated functionalized first electrode obtained in step iv) to obtain at least one dried coated first electrode which is coated with the at least one mediator polymer,

vi) curing the at least one dried coated first electrode, whereby the at least one second group of the functionalizing compound and the at least one cross-linkable group of the at least one mediator polymer are cross-linked to form the sensing layer on the electrode of the analyte sensor.

Herein, the indicated steps i) to vi) may, preferably, be performed in the given order, thereby commencing with process step i) and finishing with process step vi), wherein, however any or all of the indicated steps, in particular process steps i) and iii), may be performed at least partially concurrently and/or step iii) may be performed before step i). Further, additional process steps, whether described herein or not, may be performed, too.

In step i) an analyte sensor is provided. For the analyte sensor the embodiments and preferences described above for the analyte sensor provided in step a) of the inventive process for forming a membrane on an analyte sensor hold true. The analyte sensor comprises at least one first electrode. In

Claims

1. A process for forming a membrane on an analyte sensor, the process comprising the steps:
   a) providing the analyte sensor, wherein the analyte sensor comprises at least one substrate and comprises at least one first electrode,
   b) providing a polymer solution which comprises components
      (A) at least one first polymer which comprises at least one first cross-linkable group, wherein the at least one first polymer is a hydrophobic polymer,
      (B) at least one second polymer which comprises at least one second cross-linkable group, wherein the at least one second polymer is a hydrophilic polymer, and
      (C) at least one first solvent,
   c) contacting the analyte sensor provided in step a) with the polymer solution provided in step b) to obtain an analyte sensor which is coated with the polymer solution,
   d) drying the analyte sensor obtained in step c) to obtain a dried analyte sensor which is coated with a polymer blend which comprises the at least one first polymer and the at least one second polymer,
   e) curing the polymer blend which coats the dried analyte sensor obtained in step d) whereby the at least one first polymer and the at least one second polymer are crosslinked to form the membrane on the analyte sensor,

   wherein the at least one first cross-linkable group and the at least one second cross-linkable group are independently of one another selected from the group consisting of benzophenone groups, azide groups, anthrachinone groups, and psoralen, and wherein the at least one second polymer is different from the at least one first polymer.

2. The process according to claim 1, wherein the curing in step e) comprises at least one of heating the polymer blend and exposing the polymer blend to light.

3. The process according to claim 1 or 2, wherein component (C), the at least one first solvent, is selected from the group consisting of water, methanol, ethanol, tetrahydrofurane, and dimethyl carbonate.

4. The process according to any one of claims 1 to 3, wherein the at least one first polymer is a homopolymer.

5. The process according to any one of claims 1 to 4, wherein the at least one second polymer is a homopolymer.

6. A process for forming a sensing layer on a first electrode of an analyte sensor, the method comprising the steps:

i) providing an analyte sensor comprising at least one first electrode wherein the at least one first electrode comprises a first electrode material,

ii) reacting the at least one first electrode of the analyte sensor provided in step i) with a functionalizing compound which comprises at least one first group which is reactive towards the first electrode material and at least one second group which is cross-linkable, to obtain at least one functionalized first electrode,

iii) providing a polymer mixture comprising components

(D) at least one mediator polymer which comprises at least one cross-linkable group,

(E) at least one second solvent,

iv) contacting the at least one functionalized first electrode obtained in step ii) with the polymer mixture provided in step iii) to obtain at least one coated functionalized first electrode,

v) drying the at least one coated functionalized first electrode obtained in step iv) to obtain at least one dried coated first electrode which is coated with the at least one mediator polymer,

vi) curing the at least one dried coated first electrode whereby the at least one second group of the functionalizing compound and the at least one cross-linkable group of the at least one mediator polymer are crosslinked to form the sensing layer on the first electrode of the analyte sensor,

wherein in a first step the sensing layer is formed on the electrode of the analyte sensor and in a second step a membrane is formed according to the process of any one of claims 1 to 5 on the analyte sensor comprising the sensing layer on the electrode.

7. The process according to claim 6, wherein the first electrode material comprises at least one metal.

8. The process according to claim 6 or 7, wherein the polymer mixture provided in step iii) additionally comprises at least one enzyme.

9. The process according to any one of claims 6 to 8, wherein component (D), the at least one mediator polymer, comprises a redox mediator selected from the group consisting of a ruthenium-containing complex and an osmium-containing complex.

10. The process according to any one of claims 6 to 9, wherein component (E), the at least one second solvent, is selected from the group consisting of water, methanol. and ethanol.