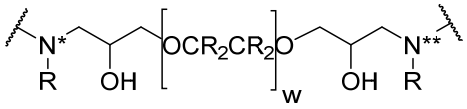
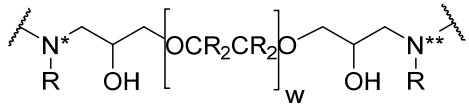
$N^*=CH(CR_2)_nS(CR_2)_mN^{**}(R)$-, $-N^*(R)(CR_2)_nCH=N^{**}$-, $-N^*(R)(C=O)(CR_2)_nCH=N^{**}$-, $-N^*(R)(CR_2)_nO(CR_2)_mCH=N^{**}$-, $-N^*(R)(CR_2)_nS(CR_2)_mCH=N^{**}$-, $-N^*=CH(CR_2)_nCH=N^{**}$-, $-N^*=CH(CR_2)_nO(CR_2)_mCH=N^{**}$-, or $-N^*=CH(CR_2)_nS(CR_2)_mCH=N^{**}$-, wherein N* represents the nitrogen at the 2 position of the 2-amino monosaccharide and N** represents the nitrogen of the n-terminal amine or the amine side chain of the one or more lysine residues of the enzyme; or R^2 is represented by the moiety: ;;

R^3 is $-N^*(R)(CR_2)_nY$, $-N^*(R)(CR_2)_n(C=O)Y$, $-N^*(R)(C=O)(CR_2)_nY$, $-N^*(R)(C=O)(CR_2)_n(C=O)Y$, $-N^*(R)(CR_2)_nO(CH_2)_mY$, $-N^*(R)(CR_2)_nS(CR_2)_mY$, $-N^*=CH(CR_2)_nY$, $-N^*=CH(CR_2)_n(C=O)Y$, $-N^*=CH(CR_2)_nO(CR_2)_mY$, $-N^*=CH(CR_2)_nS(CR_2)_mY$, $-N^*(R)(CR_2)_nCH=Y$, $-N^*(R)(C=O)(CR_2)_nCH=Y$, $-N^*(R)(CR_2)_nO(CH_2)_mCH=Y$, $-N^*(R)(CR_2)_nS(CR_2)_mCH=Y$, $-N^*=CH(CR_2)_nCH=Y$, $-N^*=CH(CR_2)_nO(CR_2)_mCH=Y$, or $-N^*=CH(CR_2)_nS(CR_2)_mCH=Y$, wherein N* represents the nitrogen at the 2 position of the 2-amino monosaccharide; or R^3 is represented by the moiety: ;

R for each occurrence is independently hydrogen, lower alkyl or hydroxyl;

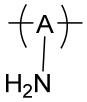
m for each occurrence is independently a whole number selected between 1-20;

n for each occurrence is independently a whole number selected between 1-20;

w for each occurrence is independently a whole number selected between 1-20; and

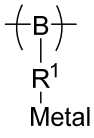
Y is a polyalkylamine comprising at least one metal complex, wherein the polyalkylamine optionally crosslinks at least two of the third repeating units.

According to an example, there is provided a redox polymer comprising a first repeating unit of Formula IIa:



IIa

and a second repeating unit of Formula IIb:



IIb

or conjugate salts thereof, wherein

each of A and B independently a 2-amino monosaccharide;

Metal is a metal complex having a redox potential lower than hydrogen peroxide under physiological conditions;

R^1 is -N*(R)(C=O)-, -N*(R)(C=O)N(R)-, -N*(R)$(CR_2)_n$-, -N*(R)$(CR_2)_n$(C=O)-, -N*(R)(C=O)$(CR_2)_n$-, -N*(R)(C=O)$(CR_2)_n$(C=O)-, -N*(R)$(CR_2)_n O(CR_2)_m$-, -N*(R)$(CR_2)_n S(CR_2)_m$-, -N*(R)$(CR_2)_n$O-, -N*(R)$(CR_2)_n$(C=O)O-, -N*(R)(C=O)$(CR_2)_n$O-, -N*(R)(C=O)$(CR_2)_n$(C=O)O-, -N*(R)$(CR_2)_n O(CR_2)_m$O-, -N*(R)$(CR_2)_n S(CR_2)_m$O-, -N*=CH$(CR_2)_n$-, -N*=CH$(CR_2)_n$(C=O)-, -N*=CH$(CR_2)_n O(CH_2)_m$-, -N*=CH$(CR_2)_n S(CR_2)_m$-, -N*=CH$(CR_2)_n$O-, -N*=CH$(CR_2)_n$(C=O)O-, -N*=CH$(CR_2)_n O(CR_2)_m$O-, or -N*=CH$(CR_2)_n S(CR_2)_m$O-, wherein N* represents the nitrogen at the 2 position of the 2-amino monosaccharide;

R for each occurrence is independently hydrogen or lower alkyl;

m for each occurrence is independently a whole number selected between 1-20; and

n for each occurrence is independently a whole number selected between 1-20.

Advantageously, the enzyme is immobilized into a thin polymer film (of the enzyme containing polymer) with redox properties on the surface of the working electrode through chemical or non-chemical means.

According to another aspect, there is provided a sensor, comprising: a substrate; a first sensor electrode on the substrate; a first sensing layer on the first sensor electrode, the first sensing layer comprising a first enzyme-containing polymer as defined herein; and a reference electrode on the substrate.

According to an example, there is provided a monitor, comprising: a receiver module configured to receive an output of a sensor as defined herein; a processor module configured to receive a first metabolite concentration value and a first control value from the receiver module, wherein the processor module is configured to: compare the first metabolite concentration value against the first control value; and generate a first signal based on the comparison.

According to another aspect, there is provided a monitor, comprising: a receiver module configured to receive a sensor output of a sensor as defined herein and a control output of another sensor as defined herein; a processor module configured to receive a first metabolite concentration value corresponding to the sensor output and a first control value corresponding to the control output from the receiver module, wherein the processor module is configured to: compare the first metabolite concentration value against the first control value; and generate a first alarm signal on a condition that a difference between the first metabolite concentration value and the first control value is above a first pre-determined value.

According to another example, there is provided a monitoring system, comprising: a sensor as defined herein; and a monitor as defined here, wherein the receiver of the monitor is arranged in use to receive an output of the sensor.

According to another aspect, there is provided a method of manufacturing a sensor, comprising: providing a substrate; forming a first sensor electrode on the substrate; forming a first sensing layer on the first sensor electrode, the first sensing layer comprising a first enzyme-containing polymer as defined herein; and forming a reference electrode on the substrate.

According to another aspect, there is provided a method for monitoring failure of a tissue on a patient, comprising the steps of:

(i) providing a first sensor as defined above on or within said tissue, said first sensor being capable of detecting and measuring the amount of a first metabolite;

(ii) providing a second sensor as defined above on a control region of said patient, said control region being separate from said tissue and wherein said second sensor is capable of detecting and measuring the amount of said first metabolite;

(iii) providing a third sensor as defined above on or within said tissue, said third sensor being capable of detecting and measuring the amount of a second metabolite and wherein said third sensor is the same as or different from the first sensor;

(iv) providing a fourth sensor as defined above on said control region of said patient, said fourth sensor being capable of detecting and measuring the amount of said second metabolite and wherein said fourth sensor is the same as or different from the second sensor;

(v) monitoring the amounts of said first metabolite measured by both said first and second sensors for a period of time; and

(vi) monitoring the amounts of said second metabolite measured by both said third and fourth sensors for a period of time.

According to another example, there is provided a method for monitoring failure of a tissue on a patient may comprise of the steps:

(i) providing a first sensor as defined herein on or within said tissue, said first sensor being capable of detecting and measuring the amount of a first metabolite;

(ii) providing a second sensor as defined herein on a control region of said patient, said control region being separate from said tissue and wherein said second sensor is capable of detecting and measuring the amount of said first metabolite;

(iii) providing a third sensor as defined herein on or within said tissue, said third sensor being capable of detecting and measuring the amount of a second metabolite and wherein said third sensor is the same as or different from the first sensor;

(iv) providing a fourth sensor as defined herein on said control region of said patient, said fourth sensor being capable of detecting and measuring the amount of said second metabolite and wherein said fourth sensor is the same as or different from the second sensor;

(v) monitoring the amounts of said first metabolite measured by both said first and second sensors for a period of time;

(vi) monitoring the amounts of said second metabolite measured by both said third and fourth sensors for a period of time;

wherein an at least 10% decrease in the amount of said first metabolite as measured by said first sensor as compared to the amount of said first metabolite as measured by said second sensor; and at least 10% increase in the amount of said second metabolite as measured by said third sensor as compared to the amount of said second metabolite as measured by said fourth sensor, is indicative that said tissue is prone to failure.

According to another aspect, there is provided a monitor, comprising: a receiver module configured to receive a sensor output of a sensor and a control output of another sensor; a processor module configured to receive a first metabolite concentration value corresponding to the sensor output and a first control value corresponding to the control output from the receiver module, wherein the processor module is configured to: compare the first metabolite concentration value against the first control value; and generate a first alarm signal on a condition that a difference between the first metabolite concentration value and the first control value is above a first pre-determined value.

According to another example, there is provided a method for monitoring failure of a tissue on a patient may comprise of the steps:

(i) providing a first sensor on or within said tissue, said first sensor being capable of detecting and measuring the amount of a first metabolite;

(ii) providing a second sensor on a control region of said patient, said control region being separate from said tissue and wherein said second sensor is capable of detecting and measuring the amount of said first metabolite;

(iii) providing a third sensor on or within said tissue, said third sensor being capable of detecting and measuring the amount of a second metabolite and wherein said third sensor is the same as or different from the first sensor;

(iv) providing a fourth sensor on said control region of said patient, said fourth sensor being capable of detecting and measuring the amount of said second metabolite and wherein said fourth sensor is the same as or different from the second sensor;

(v) monitoring the amounts of said first metabolite measured by both said first and second sensors for a period of time;

(vi) monitoring the amounts of said second metabolite measured by both said third and fourth sensors for a period of time;

wherein an at least 10% decrease in the amount of said first metabolite as measured by said first sensor as compared to the amount of said first metabolite as measured by said second sensor; and at least 10% increase in the amount of said second metabolite as measured by said third sensor as

compared to the amount of said second metabolite as measured by said fourth sensor, is indicative that said tissue is prone to failure.

According to another example, there is provided a method for monitoring failure of a tissue on a patient, comprising the steps of:

(i) providing a first sensor on or within said tissue, said first sensor being capable of detecting and measuring the amount of a first metabolite;

(ii) providing a second sensor on a control region of said patient, said control region being separate from said tissue and wherein said second sensor is capable of detecting and measuring the amount of said first metabolite;

(iii) providing a third sensor on or within said tissue, said third sensor being capable of detecting and measuring the amount of a second metabolite and wherein said third sensor is the same as or different from the first sensor;

(iv) providing a fourth sensor on said control region of said patient, said fourth sensor being capable of detecting and measuring the amount of said second metabolite and wherein said fourth sensor is the same as or different from the second sensor;

(v) monitoring the amounts of said first metabolite measured by both said first and second sensors for a period of time;

(vi) monitoring the amounts of said second metabolite measured by both said third and fourth sensors for a period of time;

wherein the amount of said first metabolite as measured by said first sensor and the amount of said first metabolite as measured by said second sensor are substantially the same; and at least 10% increase in the amount of said second metabolite as measured by said third sensor as compared to the amount of said second metabolite as measured by said fourth sensor, is indicative that said tissue is prone to failure.

According to another example, there is provided a method for monitoring failure of a tissue on a patient, comprising the steps of:

(i) providing a first sensor on or within said tissue, said first sensor being capable of detecting and measuring the amount of a first metabolite;

(ii) providing a second sensor on a control region of said patient, said control region being separate from said tissue and wherein said second sensor is capable of detecting and measuring the amount of said first metabolite;

(iii) providing a third sensor on or within said tissue, said third sensor being capable of detecting and measuring the amount of a second metabolite and wherein said third sensor is the same as or different from the first sensor;

(iv) providing a fourth sensor on said control region of said patient, said fourth sensor being capable of detecting and measuring the amount of said second metabolite and wherein said fourth sensor is the same as or different from the second sensor;

(v) monitoring the amounts of said first metabolite measured by both said first and second sensors for a period of time;

(vi) monitoring the amounts of said second metabolite measured by both said third and fourth sensors for a period of time;

wherein an at least 10% decrease in the amount of said first metabolite as measured by said first sensor as compared to the amount of said first metabolite as measured by said second sensor; and the

amount of said second metabolite as measured by said third sensor and the amount of said second metabolite as measured by said fourth sensor are substantially the same, is indicative that said tissue is prone to failure.

According to another example, there is provided a method for monitoring failure of a tissue on a patient, comprising the steps of:

(i) providing a first sensor on or within said tissue, said first sensor being capable of detecting and measuring the amount of a first metabolite;
(ii) providing a second sensor on a control region of said patient, said control region being separate from said tissue and wherein said second sensor is capable of detecting and measuring the amount of said first metabolite;
(iii) providing a third sensor on or within said tissue, said third sensor being capable of detecting and measuring the amount of a second metabolite and wherein said third sensor is the same as or different from the first sensor;
(iv) providing a fourth sensor on said control region of said patient, said fourth sensor being capable of detecting and measuring the amount of said second metabolite and wherein said fourth sensor is the same as or different from the second sensor;
(v) monitoring the amounts of said first metabolite measured by both said first and second sensors for a period of time;
(vi) monitoring the amounts of said second metabolite measured by both said third and fourth sensors for a period of time;

wherein an at least 10% decrease in the amount of said first metabolite as measured by said first sensor as compared to the amount of said first metabolite as measured by said second sensor; and an at least 10% decrease in the amount of said second metabolite as measured by said third sensor as compared to the amount of said second metabolite as measured by said fourth sensor, is indicative that said tissue is prone to failure.

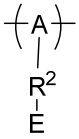
According to another example, there is provided a method for monitoring failure of a tissue on a patient, comprising the steps of:

(i) providing a first sensor on or within said tissue, said first sensor being capable of detecting and measuring the amount of a first metabolite;
(ii) providing a second sensor on a control region of said patient, said control region being separate from said tissue and wherein said second sensor is capable of detecting and measuring the amount of said first metabolite;
(iii) providing a third sensor on or within said tissue, said third sensor being capable of detecting and measuring the amount of a second metabolite and wherein said third sensor is the same as or different from the first sensor;
(iv) providing a fourth sensor on said control region of said patient, said fourth sensor being capable of detecting and measuring the amount of said second metabolite and wherein said fourth sensor is the same as or different from the second sensor;
(v) monitoring the amounts of said first metabolite measured by both said first and second sensors for a period of time;
(vi) monitoring the amounts of said second metabolite measured by both said third and fourth sensors for a period of time;

Claims

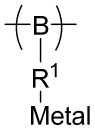
1. An enzyme-containing polymer comprising:

a first repeating unit of Formula Ia:



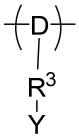
Ia,

a second repeating unit of Formula Ib:



Ib, and

a third repeating unit of Formula Ic:



Ic

or conjugate salts thereof, wherein

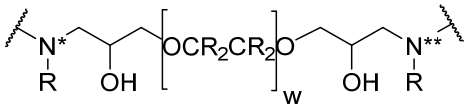
each of A, B, and D is independently a 2-amino monosaccharide;

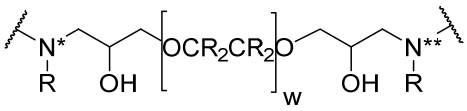
E is an enzyme comprising an n-terminal amine and optionally one or more lysine residues, wherein R^2 is covalently bonded to the n-terminal amine or the amine side chain of the one or more lysine residues;

Metal is a metal complex having a redox potential lower than hydrogen peroxide under physiological conditions;

R^1 is -N*(R)(C=O)-, -N*(R)(C=O)N(R)-, -N*(R)$(CR_2)_n$-, -N*(R)$(CR_2)_n$(C=O)-, -N*(R)(C=O)$(CR_2)_n$-, -N*(R)(C=O)$(CR_2)_n$(C=O)-, -N*(R)$(CR_2)_n$O$(CR_2)_m$-, -N*(R)$(CR_2)_n$S$(CR_2)_m$-, -N*(R)$(CR_2)_n$O-, -N*(R)$(CR_2)_n$(C=O)O-, -N*(R)(C=O)$(CR_2)_n$O-, -N*(R)(C=O)$(CR_2)_n$(C=O)O-, -N*(R)$(CR_2)_n$O$(CR_2)_m$O-, -N*(R)$(CR_2)_n$S$(CR_2)_m$O-, -N*=CH$(CR_2)_n$-, -N*=CH$(CR_2)_n$(C=O)-, -N*=CH$(CR_2)_n$O$(CR_2)_m$-, -N*=CH$(CR_2)_n$S$(CR_2)_m$-, -N*=CH$(CR_2)_n$O-, -N*=CH$(CR_2)_n$(C=O)O-, -N*=CH$(CR_2)_n$O$(CR_2)_m$O-, or -N*=CH$(CR_2)_n$S$(CR_2)_m$O-, wherein N* represents the nitrogen at the 2 position of the 2-amino monosaccharide;

R^2 is -N*(R)$(CR_2)_n$N**(R)-, -N*(R)$(CR_2)_n$(C=O)N**(R)-, -N*(R)(C=O)$(CR_2)_n$-, -N*(R)(C=O)$(CR_2)_n$(C=O)N**(R)-, -N*(R)$(CR_2)_n$O$(CR_2)_m$N**(R)-, -N*(R)$(CR_2)_n$S$(CR_2)_m$N**(R)-,

-N*=CH(CR_2)$_n$N**(H)-, -N*=CH(CR_2)$_n$(C=O)N**(R)-, -N*=CH(CR_2)$_n$O(CR_2)$_m$N**(R)-, -N*=CH(CR_2)$_n$S(CR_2)$_m$N**(R)-, –N*(R)(CR_2)$_n$CH=N**-, -N*(R)(C=O)(CR_2)$_n$CH=N**-, -N*(R)(CR_2)$_n$O(CR_2)$_m$CH=N**-, -N*(R)(CR_2)$_n$S(CR_2)$_m$CH=N**-, -N*=CH(CR_2)$_n$CH=N**-, -N*=CH(CR_2)$_n$O(CR_2)$_m$CH=N**-, or -N*=CH(CR_2)$_n$S(CR_2)$_m$CH=N**-, wherein N* represents the nitrogen at the 2 position of the 2-amino monosaccharide and N** represents the nitrogen of the n-terminal amine or the amine side chain of the one or more lysine residues of the enzyme; or R^2 is represented by the moiety:  ;

R^3 is -N*(R)(CR_2)$_n$Y, -N*(R)(CR_2)$_n$(C=O)Y, -N*(R)(C=O)(CR_2)$_n$Y, -N*(R)(C=O)(CR_2)$_n$(C=O)Y, -N*(R)(CR_2)$_n$O(CH_2)$_m$Y, -N*(R)(CR_2)$_n$S(CR_2)$_m$Y, -N*=CH(CR_2)$_n$Y, -N*=CH(CR_2)$_n$(C=O)Y, -N*=CH(CR_2)$_n$O(CR_2)$_m$Y, -N*=CH(CR_2)$_n$S(CR_2)$_m$Y, -N*(R)(CR_2)$_n$CH=Y, -N*(R)(C=O)(CR_2)$_n$CH=Y, -N*(R)(CR_2)$_n$O(CH_2)$_m$CH=Y, -N*(R)(CR_2)$_n$S(CR_2)$_m$CH=Y, -N*=CH(CR_2)$_n$CH=Y, -N*=CH(CR_2)$_n$O(CR_2)$_m$CH=Y, or -N*=CH(CR_2)$_n$S(CR_2)$_m$CH=Y, wherein N* represents the nitrogen at the 2 position of the 2-amino monosaccharide; or R^3 is represented by the moiety:  ;

R for each occurrence is independently hydrogen, lower alkyl or hydroxyl;

m for each occurrence is independently a whole number selected between 1-20;

n for each occurrence is independently a whole number selected between 1-20;

w for each occurrence is independently a whole number selected between 1-20; and

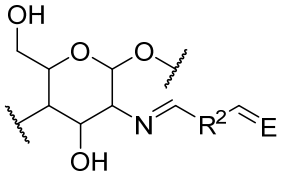
Y is a polyalkylamine comprising at least one metal complex, wherein the polyalkylamine optionally crosslinks at least two of the third repeating units.

2. The enzyme-containing polymer of claim 1, wherein the metal complex is optionally substituted ferrocenyl.

3. The enzyme-containing polymer of claim 1, wherein the molar ratio of the first repeating unit to the third repeating unit in the enzyme-containing polymer is between 1:2 to 2:1.

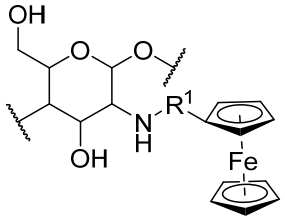
4. The enzyme-containing polymer of claim 1, wherein the 2-amino monosaccharide is selected from the group consisting of glucosamine, mannosamine, and galactosamine.

5. The enzyme-containing polymer of claim 2, wherein the first repeating unit has the Formula **IIIa**:



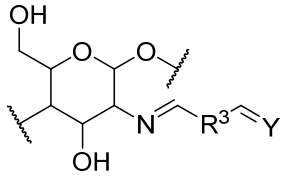
IIIa,

the second repeating unit has the Formula **IIIb**:



IIIb, and

the third repeating unit has the Formula **IIIc**:



IIIc,

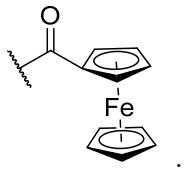
wherein

R^1 is -(C=O)-, -(C=O)$(CH_2)_n$-, -(C=O)$(CH_2)_n$(C=O)-, -$(CH_2)_n$(C=O)O-, or -(C=O)$(CH_2)_n$O-;

R^2 is -$(CH_2)_n$-;

R^3 is -$(CH_2)_n$-; and

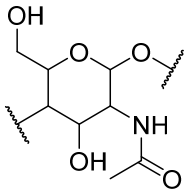
Y is a branched polyethylenimine comprising at least one primary or secondary amine covalently bonded to a moiety having the structure:



.

6. The enzyme-containing polymer of claim 5, wherein R^1 is -(C=O)-; R^2 is -$(CH_2)_3$-; and R^3 is -$(CH_2)_3$-.

7. The enzyme-containing polymer of claim 5 further comprising a fourth repeating unit of Formula IIId:



IIId.

8. The enzyme-containing polymer of claim 5, wherein the enzyme is selected from the group consisting of glucose oxidase, lactate oxidase, xanthine oxidase, cholesterol oxidase, malate oxidase, galactose oxidase, glucose dehydrogenase, lactate dehydrogenase, xanthine

dehydrogenase, alcohol oxidase, choline oxidase, xanthine oxidase, glutamate oxidase and amine oxidase.

9. A sensor, comprising:

a substrate;

a first sensor electrode on the substrate;

a first sensing layer on the first sensor electrode, the first sensing layer comprising a first enzyme-containing polymer as defined in any one of claims 1 to 8; and

a reference electrode on the substrate.

10. The sensor according to claim 9, further comprising:

a second sensor electrode on the substrate; and

a second sensing layer on the second sensor electrode, the second sensing layer comprising a second enzyme-containing polymer as defined in any one of claims 1 to 8.

11. The sensor according to claim 9 or 10, wherein the first sensing layer or the second sensing layer has a thickness of in the range of about 0.010 mm to about 0.300 mm.

12. The sensor according to any one of claims 9 to 11, further comprising:

an elongated body portion having a body axis extending centrally through the elongated body portion; and

a tip portion having a tip axis extending centrally through the tip portion, the tip portion comprising the substrate,

wherein the tip portion is disposed adjacent the elongated body portion and at an obtuse angle of between 90° to 170° between the body axis and the tip axis.

13. The sensor according to claim 12, wherein the elongated body portion comprises a fluid reservoir and an actuator, and the tip portion further comprises an inflatable member, wherein a channel is disposed between the fluid reservoir and the inflatable member, and wherein the actuator is configured to deliver a volume of fluid in the fluid reservoir through the channel to the inflatable member to inflate the inflatable member.

14. The sensor according to claim 12, wherein the elongated body portion comprises a securing pin and the tip portion further comprises a moveable member, and wherein the securing pin is configured to secure the moveable member at an activated position

15. A monitor, comprising:

a receiver module configured to receive a sensor output of a sensor as defined in any one of claims 9 to 14 and a control output of another sensor as defined in any one of claims 9 to 14;

a processor module configured to receive a first metabolite concentration value corresponding to the sensor output and a first control value corresponding to the control output from the receiver module, wherein the processor module is configured to:

compare the first metabolite concentration value against the first control value; and

generate a first alarm signal on a condition that a difference between the first metabolite concentration value and the first control value is above a first pre-determined value.

16. The monitor according to claim 15, wherein the processor module is further configured to receive a second metabolite concentration value corresponding to the sensor output and a second

control value corresponding to the control output from the receiver module, and wherein the processor module is further configured to:

compare the second metabolite concentration value against the second control value; and

generate a second alarm signal on a condition that a difference between the second metabolite concentration value and the second control value is above a second pre-determined value.

17. The monitor according to claim 16, wherein the processor module is further configured to trigger an alarm on a condition that the first alarm signal and/or the second alarm signal is generated, the alarm indicating a possibility of tissue failure.

18. The monitor according to claim 16 or 17, further comprising an output module in communication with the processor module, wherein the output module is configured to provide an indication of at least one of:

the first metabolite concentration value;

the first control value;

the second metabolite concentration value;

the second control value;

the difference between the first metabolite concentration value and the first control value;

the difference between the second metabolite concentration value and the second control value;

the difference between the first metabolite concentration value and the first control value with respect to the first pre-determined value; and

the difference between the second metabolite concentration value and the second control value with respect to the second pre-determined value.

19. A method of manufacturing a sensor, comprising:

providing a substrate;

forming a first sensor electrode on the substrate;

forming a first sensing layer on the first sensor electrode, the first sensing layer comprising a first enzyme-containing polymer as defined in any one of claims 1 to 8; and

forming a reference electrode on the substrate.

20. The method according to claim 19, further comprising:

forming a second sensor electrode on the substrate; and

forming a second sensing layer on the second sensor electrode, the second sensing layer comprising a second enzyme-containing polymer as defined in any one of claims 1 to 8.

21. A method for monitoring failure of a tissue on a patient, comprising the steps of:

(i) providing a first sensor according to claims 9 to 14 on or within said tissue, said first sensor being capable of detecting and measuring the amount of a first metabolite;

(ii) providing a second sensor according to claims 9 to 14 on a control region of said patient, said control region being separate from said tissue and wherein said second sensor is capable of detecting and measuring the amount of said first metabolite;

(iii) providing a third sensor according to claims 9 to 14 on or within said tissue, said third sensor being capable of detecting and measuring the amount of a second metabolite and wherein said third sensor is the same as or different from the first sensor;

(iv) providing a fourth sensor according to claims 9 to 14 on said control region of said patient, said fourth sensor being capable of detecting and measuring the amount of said second metabolite and wherein said fourth sensor is the same as or different from the second sensor;

(v) monitoring the amounts of said first metabolite measured by both said first and second sensors for a period of time; and

(vi) monitoring the amounts of said second metabolite measured by both said third and fourth sensors for a period of time.

22. A monitor, comprising:

a receiver module configured to receive a sensor output of a sensor according to claims 9 to 14 and a control output of another sensor according to claims 9 to 14;

a processor module configured to receive a first metabolite concentration value corresponding to the sensor output and a first control value corresponding to the control output from the receiver module, wherein the processor module is configured to:

compare the first metabolite concentration value against the first control value; and generate a first alarm signal on a condition that a difference between the first metabolite concentration value and the first control value is above a first pre-determined value.

23. The monitor according to claim 22, wherein the processor module is further configured to receive a second metabolite concentration value corresponding to the sensor output and a second control value corresponding to the control output from the receiver module, and wherein the processor module is further configured to:

compare the second metabolite concentration value against the second control value; and generate a second alarm signal on a condition that a difference between the second metabolite concentration value and the second control value is above a second pre-determined value.

24. The monitor according to claim 22, wherein the difference between the first metabolite concentration value and the first control value is at least 10% different from the first pre-determined value.

25. The monitor according to claim 23, wherein the difference between the second metabolite concentration value and the second control value is at least 10% different from the second pre-determined value.