Biocompatible Membranes with Special Functions for Biosensor’s Application

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Biocompatibility is indispensable to biosensors for in vivo purpose. To those for in vitro applications biocompatibility can also promote their stability and lifetime. 2-Methacryloyloxyethyl phosphorylcholine, abbreviated as MPC, is an inert biocompatible material. Biocompatible membranes with special functions including diffusion-limiting effect, selective permeability, and the capability of immobilizing enzymes were obtainable by the copolymerization of MPC with other monomers. These membranes were applied to fabricate needle-type glucose sensors. The sensors were conferred with a wide workable range, good biocompatibility, remarkable long-term stability, and the ability of curtailing interfering responses upon application of these specially functionalized biocompatible membranes.

Key word: MPC, biocompatibility, diffusion-limiting effect, selective permeability, needle-type, glucose sensor.

Preface

Biocompatibility is indispensable in developing a biosensor for in vivo purpose or for in vitro determination of biofluid samples. In the former cases, biocompatibility prevents the organism from being elicited immune reactions. In the later case, biocompatibility reduces or inhibits adhesion of bio-components on active surface of the sensor.

There are two kinds of biocompatible materials, active (positive)1, 2) and inert (negative)3, 4). Neither of them elicit an immune reaction but the former have a disadvantage in that components of biological fluids adhere to them. These act as a barrier to the diffusion of analyte into the biological layer of a biosensor and consequently they reduce its response. 2-Methacryloyloxyethyl phosphorylcholine (MPC) is an inert biocompatible material. It can copolymerize with methacrylate compounds, for example n-butylmethacrylate (BMA). The synthesis of MB, the copolymer of 2-methacryloyloxyethyl phosphorylcholine (MPC) and n-butylmethacrylate (BMA), has been described previously5, 6). This polymer was selected as the component responsible for biocompatibility for the task of constructing membranes with spe-
special functions suitable for biosensor’s application. The structural formula of MB is presented in Fig. 1.

Biosensor is a device that intimately associates a biological sensing element and a transducer. There are several methods to cooperate the sensing element and a transducer. The most convenient one is to fit the bio-material in a membrane form intimately onto the active surface of a transducer, an electrode for example. Three elements are required for the construction of a biosensor: a recognition element composed of biological material that react selectively with the specific substrate; a conversion element for converting the related physicochemical information from the biocatalytic reaction into electrical signals; and an element for recording these electrical signals. The general concept of a biosensor is shown in Fig. 2.

The major benefits of a biosensor can be illustrated as (1) specific determination of the expected substrate from a sample with complex composition. (2) non-invasive determination. (3) reagentless determination. (4) reusability. (5) on time and on line monitoring. (6) implantability. (7) easy operation and simple instrumentation. The most significant advantage of a biosensor is that it is conferred high level of selectivity from the biological sensing element and at the same time bestowed fast and accurate response from the transducer. The selectivity enables a biosensor to directly determine a specified substrate, or some closely related substrates, in a sample with complex composition. This action effectively retrenches fastidious and time consuming procedures of isolation and purification. The transducer, on the other hand, enables the immediate conversion of various physicochemical signals of biological reactions such as chemicals, heat, emission and oscillation into electrical signal that can be recorded simultaneously.

On the basis of these benefits the studies of biosensor has been motivated by its practical instinct with wide spectrum of application. Most of the impetus comes from medical requirements. Many biosensors have been developed for medical purpose. Glucose sensors attracted more attention than others because the sample of blood sugar is the most abundant in clinical laboratories. There are increasing requirements for both in vitro and in vivo medical applications to glucose sensors. The former is expected to be used to determine abundant samples in clinical laboratories. The later, however, is aimed at associating a glucose sensor with an insulin infusion system.

Biocompatible membranes with special functions were applied to develop needle-type biosensors that are suitable for medical applications. Glucose was chosen as the analyte because it is the most abundant sample in clinical laboratories. Considerations from many aspects including the

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**Fig. 2 General description of the concept of biosensors.**

characteristics of the sensor itself, the material and the shape of the sensor, the structure of the electrode, the instrumentation of the operation system and, especially the biocompatibility of the sensor in biological fluids were taken to design and construct the sensors. Needle-type glucose sensing system, including the sensors themselves and instrumentations of the operation system, that can fit the requirement of determining glucose in serum and whole blood were constructed. All the techniques adopted to fabricate the glucose sensing system was carefully selected on the basis that there are capability of applying them to develop other biosensors for medical applications. The concepts and methods described here are expected as the basis of further studies in developing useful biosensors that are applicable to many other fields.

**Preparation and characterization of MPC, MB, and MBC**

Detail procedure of synthesizing 2-methacryloyloxyethyl phosphorylcholine (MPC) has been described previously. The reactions involved are summarized in Fig. 3. MB is the copolymer of MPC and n-butylmethacrylate (BMA). An initiator, 2, 2'-azoisobutyronitrile (AIBN), and the desired amount of MPC and BMA were dissolved in methanol. This solution was sealed in a glass ample with argon atmosphere and then heated in an oil bath to complete the copolymerization.

MB is a copolymer with good membrane-forming property. After cast on a plate or dip-coated on a rod only a few minutes for solvent evaporation is required to form the MB membrane. The
thrombogenicity in addition to the hydration and the permeability of the MB membrane has also been described. It showed a reduced thrombogenicity. Relatively few platelets bound to MB membrane when compared with BMA membrane after contacting with platelet rich plasma. The adherence of platelet has been reported as one of the initiating step of immune reactions. Relatively few platelets bound to it indicated good compatibility to blood.

A glucose sensor constructed by cooperating an immobilized glucose oxidase membrane and a \( \text{H}_2\text{O}_2 \) probe was found to have a dynamic range no wider than 100 mg/dl. The glucose concentration in human was reported as 50-120 mg/dl for non-diabetics and may as high as 600 mg/dl for diabetics. The membranes of cellulose acetate (CA) and its derivatives were often used to extend the dynamic range of a biosensor. MB membrane is biocompatible but with no effect for extending the dynamic range. However, the MBC membrane prepared by casting a mixture of MB and CA can effectively extend the dynamic range of a biosensor. The extent to which the dynamic range will be extended is dependent on the concentration of CA used to prepare the MBC membrane.

The compatibility of the MBC membrane to blood has also been evaluated. The carotid artery of a rabbit weighing about 3 kg was cannulated with PVC tubing. Fresh blood (90 ml) was collected in a disposable cylinder containing 10 ml of 3.8% (w/v) sodium citrate solution. Immediately afterwards the blood was centrifuged at 750 rpm (90 g) for 15 minutes. The supernatant was collected as platelet-rich plasma (PRP). The precipitate was centrifuged again at 2800 rpm (1250 g) for 10 minutes. The second supernatant contained less platelet and was called platelet-poor plasma (PPP). The platelet content of PRP was adjusted to approxi-
A CA solution and the MBC solution were cast onto a piece of Nuclepore polyester filter (pore size 0.2 μm, Nuclepore Co., CA., USA), individually, and dried in air at room temperature. When dry the filters were immersed in the PRP for either 1 or 3 hours and then transferred to a saline solution containing 2.5% glutaraldehyde to reinforce the immobilization of bound platelet. The filters were rinsed, dried, coated with gold, and then the surface was investigated using a scanning electron microscope.

Differences in the number of platelet bound and the morphology thereof, between a MBC membrane and a CA membrane, are shown in Fig. 4. After contact with PRP for one hour, relatively few platelet adhered to the surface of the MBC membrane (Fig. 4-a). By contrast a relatively large number of platelet adhered to the surface of the CA membrane (Fig. 4-b). After immersion in PRP for 3 hours the number of platelet attached to the MBC membrane was still relative few and no morphological change in them was observed (Fig. 4-c). This was in marked contrast to the appearance of platelet bound to the CA membrane (Fig. 4-d). These results suggest that this material exhibits a high degree of biocompatibility.

Application of the MBC membrane to fabricate a needle-type glucose sensor

A needle-type H₂O₂ probe with two-electrode configuration was prepared. A hypodermic needle made of stainless steel was electroplated with platinum and used as the counter/reference electrode. A piece of platinum wire (D=0.3 mm) was insulated with FEP heat-shrink tube and had the tip cut at an 18° angle to expose the metallic sur-
face. It was then polished and used as the working electrode. The procedure for constructing the probe is shown in Fig. 5.

A Nafion membrane and an immobilized GOD membrane were coated successively onto the metallic surface of the working electrode as described previously. After the enzyme was crosslinked with glutaraldehyde and entrapped by photocrosslinking PVA-SbQ, the tip of the electrode was dipped into the MBC solution for 10 seconds and then air dried. The electrodes were stored at 4°C in a refrigerator until use.

Characterization and application of the sensor with the MBC membrane

A batch operation system composed of a potentiostat, a circulating water bath, a water-jacketed glass reactor, a magnetic stirrer with stirring bar, and a chart recorder, as shown in Fig. 6, was used in subsequent determinations.

The response, reproducibility, selectivity, and stability of the sensor along with the effects of temperature, pH, and metallic ions on response of the sensor were studied. The sensor showed a wide dynamic range in addition to its biocompatibility because the presence of a MBC membrane as the outermost layer of the multi-layer membrane system of the sensor. The dynamic range extended to 1000 mg/dl (≈55.5 mM) glucose with a response of 50 nA to 100 mg/dl glucose. However, by using various concentration of CA to prepare the MBC membrane the dynamic range of the sensor can be properly adjusted between 200 and 1000 mg/dl glucose. The narrower the dynamic range the higher the response. The sensor showed a rapid response. No more than 120 seconds was required for reaching 95% response. The sensor was used to assay the same glucose solution repeatedly to investigate its reproducibility. The relative errors of 12 successive determinations for samples of 150 and 100 mg/dl glucose were 2.1 and 1.2%, respectively.

The relative responses of the sensor at various pH levels in different buffers were also studied. The highest response was found in phosphate buffer at pH 7.0, indicating a high response of the the sensor in blood (pH 7.2-7.6). The response increased with temperature from 6 to 50°C. The response at lower temperature was unchanged after the sensor had been tested at 50°C. This suggested a good stability of the sensor at the body temperature of human being. The effects of metallic ions usually encountered in biological fluids including calcium, magnesium, iron and copper were tested. Of these only copper (II), at a concentration slightly higher than that found in serum, caused a reduction of 7.8% in the response of the sensor. Silver (I) and mercury (II) caused the response of the sensor to drop by 96.1% and 61.4%, respectively. Inhibition of immobilized glucose oxidase by silver (I) and mercury (II) has been studied previously. These ions, however, are at most only present at a very low concentration in biological fluids.

To examine the stability, the sensor was situated in a 37°C glass reactor containing 5 ml of control serum with 0.1% (w/v) sodium azide (NaN₃) as preservative. The response of the sensor was recorded continuously for 37.5 hours. The same experiment was also performed for a glucose sensor on which CA but not MBC was used as the outermost layer of its multi-layer membrane system. In addition, 10 μl of the control serum was taken from the reactor at 2.5 hour intervals and...
analyzed by the GOD kit. The results are shown in Fig. 7. The response of the sensor with MBC membrane remained stable for 37.5 hours. During which period data from the sensor showed good agreement with that from GOD kit. The response of the sensor with a CA membrane remained stable for 15 hours. Only 53.6% of the original response remained after 37.5 hours.

Twelve serum samples were assayed for glucose with both the sensor and the autoanalyzer. The data from the two methods showed good agreement. The correlation coefficient was 0.982 ($y = 1.0463x - 9.6687$).

**Preparation of MBG and the biocompatibility of GOD-MBG-CTA**

MBG is a biocompatible polymer with epoxy groups. It was prepared by the copolymerization of 2-methacryloyloxyethyl phosphorylcholine (MPC), n-butylmethacrylate (BMA), and glycidylmethacrylate (GMA). An initiator 2, 2'-azoisobutyronitrile (AIBN) and the desired amount of MPC, BMA, and GMA (mole ratio 4 : 4 : 2) were dissolved in methanol. This solution was sealed in a glass ampule with argon atmosphere and then heated in an oil bath at 60°C for 4 hours to complete the copolymerization. The copolymer was precipitated in ether, dissolved in isopropanol, and then stored at 4°C until use. The structural formula of MBG is presented in Fig. 8. An enzyme, for example glucose oxidase (GOD), can be immobilized onto MBG via the reaction between the amino groups of GOD and the epoxy groups of GMA. The reaction of forming a covalent bonding between an enzyme molecule and the MBG is shown in Fig. 9. GOD- MBG solution was prepared by mixing MBG solution with GOD solution. It was incubated at 37°C for 1 hour to complete the reaction between the amino groups of GOD and the epoxy groups of MBG. Cellulose triacetate (CTA)
solution was then mixed with the GOD-MBG solution with vigorous stirring to form a viscous GOD-MBG-CTA mixture.

The GOD-MBG-CTA solution and the CTA solution were spread individually on telephthalate disks. The compatibility to blood of them were investigated by the same procedure as used for evaluating the biocompatibility of MB membrane. After contacting with the PRP and whole blood for 1 hour no more than 100 platelets or blood cells adhered to the surface of the GOD-MBG-CTA membrane in 1 mm². In sharply contrast to the GOD-MBG-CTA membrane, there are numerous platelets and blood cells adhered to the surface of the CTA membrane. The ability of the GOD-MBG-CTA to inhibit the adherence of platelets and blood cells suggested a high level of biocompatibility of it.

Construction of a needle-type probe with 3-electrode configuration and the application of the GOD-MBG-CTA membrane to fabricate a needle-type glucose sensor

The probe with 2-electrode configuration is advantageous by its simple construction. However, a drift of about 100 mV to the polarizing potential was observed after the sample injection in a determination. This drift creates a possibility of inaccuracy to the sensor. For surmounting this problem a needle-type probe with 3-electrode configuration was constructed.

A hypodermic needle made of stainless steel (OD =1.2 mm, ID=1.0 mm) was used as the counter electrode. A piece of platinum wire (D=0.3 mm) was insulated with Teflon tube. The Teflon tube was stripped to form a cavity. This was achieved by making a circular cut on the Teflon tube 1 mm from the tip and then pull the tube out to create a cavity of 0.5 mm wide. It was used as the working electrode. A piece of Teflon coated silver wire (D=0.127 mm) was created a cavity by the same process. Silver was converted to Ag/AgCl by dipping in a H₂O₂-HCl solution (1 M H₂O₂ and 1 M HCl at 1 : 1 ratio) and used as the reference electrode. A Nafion membrane was coated onto the metallic surface of the working electrode by dropping 2 μl of the Nafion solution into the cavity of it and then air dried at room temperature. The GOD-MBG-CTA membrane was then coated onto the working electrode by the same operation.

The reference and the working electrodes were inserted into the interior of the counter electrode. Epoxy resin was used to fix them at the position. The electrodes were stored at 4°C in a refrigerator until use. The schematic diagram of the sensor is shown in Fig. 10.

Characterization and application of the sensor with the GOD-MBG-CTA membrane

The dynamic range of the sensor coated with a Nafion membrane and a GOD-MBG membrane without containing CTA was 0.2-60 mg/dl glucose. The dynamic range of the sensor was extended to 1-450, 2-700, and 5-1000 mg/dl glucose by mixing the GOD-MBG solution with 2, 3, and 4% (w/v) CTA solutions, respectively, at a 1 : 1
The ability to extend the dynamic range of the sensor demonstrate the diffusion-limiting effect of the GOD-MBG-CTA membrane to glucose. The sensor using 2% CTA solution to prepare the GOD-MBG-CTA membrane has good sensitivity and a dynamic range that is wide enough for most clinical samples. It was therefore used for subsequent experiments.

The response of the sensor to 100 mg/dl glucose at various temperatures were studied. The response increased with temperature from 2 to 37°C. When taking the response at 37°C as 100, the response at 2, 5, 10, 20, and 30°C was 10.3, 13.7, 28.8, 54.1, and 82.9%, respectively. At all temperatures the time needed for reaching 95% response was no more than 90 seconds.

The relative response of the sensor at blood's pH range were investigated. The sensor showed the highest response at pH 7.2. The differences in responses from pH 7.2 to 7.6 were less than 4%.

Calcium, magnesium, iron and copper are the main metallic ions encountered in serum. Of these copper (II), at a concentration slightly higher than found in serum, caused a reduction of 9.2% in the response of the sensor. Silver (I) and mercury (II) caused the response of the sensor to drop by 31% and 15%, respectively.

The relative response of the sensor to maltose, galactose, and mannose were 2.1, 0.9, and 1.4, respectively, when the response to glucose was taken as 100. Reactions of GOD with galactose, maltose, and mannose have been reported. The relative reaction rate were reported as 100, 0.14, 0.19 and 0.98 for glucose, galactose, maltose, and mannose, respectively. According to the operation data sheet provided by the supplier, the GOD used in this study also contained the following contaminants: maltose, glycogenase, invertase, amylase, and galactose oxidase. It is likely that contaminants in GOD should take the major responsibility for slightly higher response of the sensor to galactose, maltose, and mannose. Sugars other than glucose, however, are only present at a very low concentration in biological fluids.

The sensor was used to measure a glucose solution repeatedly to investigate its reproducibility. The relative error for a sample of 100 mg/dl glucose was 2.6% for 32 successive determinations.

To examine the stability in serum, the sensor was situated in a 37°C glass reactor containing 5 ml of control serum with 0.1% (w/v) sodium azide (NaNO₃) as a preservative. The response of the sensor was recorded continuously for 36 hours. During this period 10 µl of the control serum was taken from the reactor at 2 hours' interval and analyzed by the GOD kit. The response of the sensor remained stable for 36 hours. During this period the data from the sensor showed good agreement with that from GOD kit.

Serum samples were assayed for glucose with both the sensor and an autoanalyzer. The correlation coefficient between the data from the two methods was 0.970 (y = 0.986x + 3.197, n = 15).

**Preparation and characterization of the MAC membrane**

A multifunctional membrane, MAC, with biocompatibility, diffusion-limiting effect and ability to curtail the responses of a H₂O₂ probe to ascorbate and urate was prepared. It was composed of MB, AB, and CTA, where MB is the copolymer of MPC and BMA; AB is the copolymer of acrylamide-2-methylpropane sulfonic acid (AMPS) and BMA; CTA is cellulose triacetate. The structural formula of AB is shown in Fig. 11. MAC so-
Solution was prepared by mixing MB solution (10% w/v in methanol), AB solution (5% w/v in isopropanol) and CTA solution (2-4% w/v in 1, 1, 2, 2-tetrachloroethane) at a 1:1:2 ratio.

The compatibility of the MAC membrane to blood has also been investigated. Difference among a CTA, an AB-CTA and the MAC membranes in the quantity of platelet bounded on the surface was exactly observed. After contacting with PRP for one hour, no more than 50 platelet adhered to 1 mm² of the MAC membrane. By contrast numerous platelet adhered to the surface of the cellulose acetate and the AB-CTA membranes. These results suggest that the MAC membrane, owing to the MPC component, exhibits a high degree of compatibility to blood.

2 µl of the GOD solution composed of 1 mg GOD (138 U/mg), 5 mg BSA, 100 mg distilled water and 100 mg PVA-SbQ was dropped on the metallic surface of the working electrode. The electrode was then exposed to a fluorescent lamp for 10 minutes to induce photocrosslinking of PVA-SbQ. 2 µl of the MAC solution was then dropped over the enzyme membrane and air-dried for 30 minutes at room temperature.

Calibration curves of the sensor coated with immobilized GOD membrane only and those further coated with MAC membranes containing various concentration of CTA were studied. The dynamic range of the sensor with only immobilized GOD membrane was 0.2-50 mg/dl glucose. The dynamic range of the sensor was extended to 2-200, 5-450 and 5-650 mg/dl glucose after being coated with MAC membranes prepared by using of 1, 2 and 3% (w/v) CTA solutions. The ability to extend the dynamic range of the sensor demonstrated the diffusion-limiting effect of the MAC membrane. The working range of the sensor using 2% CTA, 5-450 mg/dl, is wide enough for most clinical samples and was used for subsequent experiments.

The responses of the bare electrode and the sensor with various membrane to ascorbate (2 mg/dl) and urate (10 mg/dl) are shown in Fig. 12. The bare electrode responded strongly to ascorbate and urate. The responses to ascorbate and urate were reduced to 21% and 39%, respectively, after the working electrode was coated with the immobilized GOD membrane. Both the responses to ascorbate and urate were reduced to zero after the working electrode was further coated with the MAC membrane. The results obtained in this section ensured the capability of the MAC membrane to prevent the sensor from being interfered with ascorbate and urate in blood.

Characterization of the sensor with the MAC membrane

In addition to a rapid response (<90 sec. in batch operation), good reproducibility (RE<5%), good stability (more than 36 hours continuously in glycolyzed heparinized whole blood) and a wide dynamic range (5-650 mg/dl glucose), the sensor ex-
hibited superior thermostability. Fig. 13 presents the response graphs of the sensor at 50 and 37°C alternatively for five repeats. The response graphs were maintained almost the same during the alternative heating and cooling processes. The response of the sensor maintained unchanged after being incubated in 50°C waterbath for 1 hour. In contrast the free glucose oxidase solution lost more than 90% of its original activity under the same treatment. These results indicated the thermostability of the enzyme was significantly improved by the protective effect of the MAC membrane and the immobilization process used in this study.

The sensor was used to assay the same glucose solution repeatedly to investigate the reproducibility. The relative error for a sample of 100 mg/dl glucose was 3.6% for 32 successive determinations.

The effects of some metallic ions on response of the sensor have also been studied. Calcium, magnesium, iron, zinc and copper are the main metallic ions encountered in serum. Of these only calcium (I), at a concentration slightly higher than that normally found in serum, caused a reduction of 6.9% to the response of the sensor. Inhibition of immobilized GOD by silver (II) and mercury (II) has been studied previously. However, they caused no reduction to the response of the sensor coated with the MAC membrane. The free enzyme in solution, as a comparison, lost 86.2% of its original activity under the same Ag (I) concentration.

To examine the stability in continuous determination, the sensor was located in a 37°C glass reactor containing 5 ml of the glycolyzed whole blood with 0.1% (w/v) sodium azide (NaN₃) as preservative. After two hours glucose was injected to bring to a concentration of 100 mg/dl. After 16 hours another injection was carried out. The response of the sensor was recorded continuously for 36 hours. On the other hand 10 μl samples were taken from the reactor at 2 hours’ interval and analyzed by the GOD kit. The response of the sensor remained stable for 36 hours. During which period data from the sensor showed good agreement with that from GOD kit.

The sensor was used to determine glucose in serum. The data obtained from the sensor showed good agreement with that from a clinical autoanalyzer (y=0.92504x+21.133, R=0.973, n=13).

**Conclusion**

Biocompatibility, a wide workable range, firm immobilization of enzyme, and the ability of curtail the responses of a sensor to interfering materials are common requirements for constructing biosensors that are applicable to undiluted biological fluids in vitro or for in vivo purpose. To meet these requirements biocompatible membranes with special functions were prepared and applied to fabricate needle-type glucose sensors.

MBC membrane, prepared by mixing CA with the copolymer of MPC and BMA, possessing both biocompatibility and a diffusion-limiting effect to glucose. Biocompatibility of it was investigated by examining its surface after immersion in platelet rich plasma and comparing them with a CA membrane treated in the same way. This demonstrated that relatively few platelet adhered to the MBC membrane and that those did failed to exhibit any discernible morphological change. The diffusion limiting effect of it was demonstrated by the extension in dynamic range which it conferred on the sensor. Details of a needle-type glucose sensor made in...
our laboratory have already been reported". This sensor showed good reproducibility and stability and was used in serum and whole blood, but it was not used in vivo because of its lack of biocompatibility. In this paper an attempt to surmount this deficiency was made by coating the sensor with the MBC membrane. The result was a sensor that exhibited good response characteristics, good reproducibility and good stability in blood.

Another copolymer composed of MPC, BMA, and GMA was synthesized. This copolymer, abbreviated as MBG, bears epoxy groups which enable it to immobilize enzyme through the covalent bonding between its epoxy group and the amino groups of an enzyme molecule. It also showed good biocompatibility and good membrane-forming property. Glucose oxidase (GOD) was immobilized onto MBG and then mixed with CTA solution. This mixture, GOD-MBG-CTA, was coated onto a platinum electrode to construct a needle-type glucose sensor.

Biocompatibility of the GOD-MBG-CTA membrane was investigated by immersing it in platelet rich plasma or whole blood for one hour and then examining its surface with electron microscope. This demonstrated that, comparing with a CTA membrane, relative few platelet or blood cell adhered to it. The GOD-MBG-CTA membrane also showed the ability to deduct the diffusion rate of glucose through it. This action contributed wider dynamic range to the sensor. A sensor that exhibited good response characteristics, good reproducibility, good stability in blood, and a wide workable range was obtained by the application of this membrane. This suggested that this membrane is potential for constructing biosensors applicable to undiluted biological fluids. Application of this membrane to fabricate other biosensors should be expectable.

A multifunctional membrane suitable for biosensor's application that can offer the sensor with biocompatibility, a wide workable range, and the ability to curtail interferences from ascorbate and urate was also prepared. The biocompatibility of it was mainly donated from the MPC molecule. The fact that platelet hardly adsorb on the MAC membrane certified its blood compatibility. The ability to curtail interference from ascorbate and urate was obtained from the negatively charged AMPS molecule. The capability to extend the working range was endowed by the lower diffusion rate of glucose through CTA membrane. The combination of those constituents succeeded a membrane which can confer several good characteristics to biosensors.

A needle-type probe using a platinum wire, a Ag/AgCl wire, and a stainless steel hypodermic needle as the working, the reference, and the counter electrode, respectively, was constructed. Glucose oxidase was chemically crosslinked with glutaraldehyde and then entrapped by a photocrosslinkable polyvinyl alcohol with stilbazolium group, PVA-SbQ. This procedure immobilized high density of the enzyme firmly in the membrane. High response and good stability of the sensor was consequently achieved. Over the immobilized enzyme membrane on the working electrode was further coated with the MAC multifunctional membrane. A needle-type glucose sensor with characteristics suitable for medical application was thus completed. The sensor showed characteristics such as biocompatibility, good reproducibility, good thermal stability and the ability to escape from being interfered with constituents of blood. The MAC membrane, being coated over the immobilized enzyme membrane but did not react with the enzyme, is expectable to be applied to construct other biosensors.

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Reference

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第53回電気透析および膜分離技術研究会

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協賛：日本膜学会ほか

日時：平成5年11月30日（火）14：00～17：00

会場：東京大学生産技術研究所第1会議室 東京都港区六本木7-22-1 電話 03-3402-2631

交通]地下鉄千代田線乃木坂または地下鉄日比谷線六本木下車

演題：1. 電気透析法による新しい造水システム （旭硝子）滋野利勝
2. 米国アリゾナ州ユマ RO 脱塩プラントの運転状況について （横国大・工）谷口良雄
3. バイポーラー膜の基礎 （東工大・工）谷岡明彦

研究会参加費：無料
懇親会参加費：3,000 円

参加申込方法：葉書に「第53回電気透析および膜分離技術研究会参加申込」と題記し、氏名、所属、連絡先を明記のうえ、下記へ御連絡下さい。なお、懇親会参加ご希望の方はその旨を明記して下さい。

参加申込締切：平成5年11月22日（月）

申込先：〒256 小田原市京町4-13-20 日本たばこ産業（株）海水総合研究所 田中良修（電話 0465-47-3161）