

## Mini Review Article

# Nanosensors Based on Lipid Films

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## Abstract

This review provides information and details about the construction of nanosensors based on lipid membranes that can be utilized to monitor toxicants in food, environmental pollutants, and analytes of clinical interest. Nanosensors based on lipid films have been used to rapidly detect a wide range of these analytes, and can offer several advantages towards analytical instrumentation such as rapid response times, high sensitivity and selectivity, portability for in the field uses and small size. A description of the preparation of these devices for the rapid detection of toxicants in foods, environmental pollutants, and analytes of clinical interest is provided in this review.

**Keywords:** Nanosensors; Lipid films; Potentiometry

## Introduction

A nanobiosensor is an analytical device having a small size that detects and analyses a sample and provides its chemical concentration and composition. A chemical nanosensor is composed of two main parts: a biological element that chemically detects the unknown compound and a physical transducer such as electrical, optical, or piezoelectric. The advantages of nanosensors compared to classical analytical devices, such as liquid and gas chromatography are plenty and include faster response times, higher throughput of samples, smaller size, and portability for field measurements. It is also cheaper and personnel do not require training for its use.

Chemosensors are similar to biosensors but are composed of a synthetically prepared molecule instead of a biological element. They recognize small molecules or metal ions by binding to them. The synthesis, design, and applications of Chemosensors are of special interest for the detection of analytes.

Nanobiosensors are based on the merging of nanotechnology with biosensors. Such materials include graphene, carbon nanotubes, and nano wires. Metal-based nanoparticles are also excellent hosts for the construction of electrical and optical devices that can be applied to detect nucleic acid sequences. Various Nanomaterials have been explored and their properties were analyzed for possible applications in biosensors. Nanobiosensor technology research has prompted the construction of an increasing number of novel devices.

This paper addresses the fabrication of nanosensing devices composed of lipid membranes that have been used and applied to rapidly detect toxic substances in food, environmental pollutants, and

analytes of clinical interest. Figure 1 provides a schematic of a lipid-based biosensor on a graphene electrode that has been used for the potentiometric detection of urea [1].

## Methods for Construction of Nanosensors Based on Lipid Membranes

During the last 10 years, the preparation of stabilized lipid membranes based devices that cannot collapse due to an electrical or mechanical shock and are stabilized in air has been reported in the literature. Below we report the techniques for the construction of nanosensors that are based on lipid films with advantages such as fast response times, nano size high selectivity and sensitivity and are stabilized in air.

### Metal supported lipid layers

Tien and Salam on have reported in the literature a system for the construction of Stabilized Bilayer Lipid Membrane (SBLM) at the end of Teflon coated metallic wire which was freshly cut [2]. This technique was relied on the interaction of an Amphiphatic lipid molecule with a nascent metallic surface. This Teflon-coated stainless steel metal wire had a diameter of 0.1 mm - 0.5 mm and its end was dipped in a lipid solution which was prepared with chloroform as a solvent and its end was cut with a guillotine which was immersed, in the solvent. An immersion of the wire in a 0.1 M KCl followed, so that the lipid membrane becomes bilayer.

SBLMS have been fully characterized [2-5]. The diameter and composition of the wires have an important impact on the time of the bilayer formation [6,7]. The diameter of the silver wire should be between 0.5 mm to 1.0 mm and the solvent used should be hexane and not decane because the latter solvent could be retained in the structure of the bilayer and provide irreproducible results.

### Stabilized lipid films formed on a glass fiber filter

The preparation of stabilized in electrolyte lipid membranes was reported by Nikolelis group and these membranes were constructed on GF/F glass microfiber (0.9 cm in diameter and 0.7 μm nominal pore size) filters. The lipids used were previously described. No receptor was used in these detections. The stable in electrolyte solution lipid films were prepared as follows: 10 μL of a lipid solution in hexane was positioned at the electrolyte surface in the cylindrical cell and the level of the electrolyte was brought below the hole of the partition and then

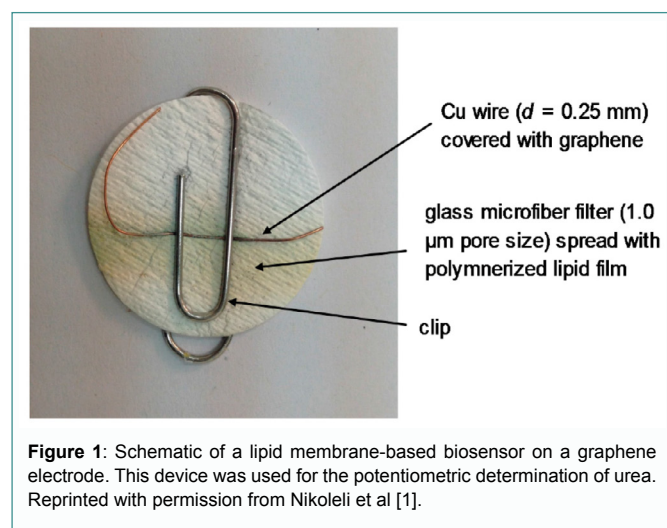
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raised again within a few seconds. Once the lipid membranes were formed, the current was at the pA and the injection of gramicidin D shows that these membranes were bimolecular.

### Polymer-supported bilayer lipid membranes

The use of a polymer-supported lipid film has been used to stabilize lipid membrane based devices in the air for periods of over one month [8].

The preparation of stabilized in air lipid membranes was reported by Nikolelis group [8-10]. The lipids used were previously described. No receptor was used in these detections. The polymer stable in air lipid membranes were constructed as previously has been described [8-10] and is as follows: 0.07 mL of methacrylic acid, 0.8 mL of ethylene glycol dimethacrylate, 8 mg of 2, 2'-azobis-(2-methylpropionitrile) and 1.0 mL of acetonitrile are added in 0.8 mL of a suspension that contained 4% w/v DPPC in a solvent of n-hexane [which evaporates and the lipid membranes are "solvent-free"). Then nitrogen is allowed to pass through this mixture and a sonication follows. A volume of 0.15 mL of this suspension is placed on the micro filter (Whatman, UK, GF/F microfiber glass disk having diameter of 0.9 cm and pore size of 0.7  $\mu\text{m}$ ) and the filters are irradiated with a UV deuterium lamp. The experimental instrumentation was the same as in Figure 1. These films were stabilized and could be stored in air for at least 1 month.



### Polymeric lipid membranes supported on graphene microelectrodes

Our group has prepared an electrode that was composed from a lipid film on a copper wire that contained graphene nanosheets [1]. These nanobiosensors were utilized for the fast monitoring of food and environmental toxicants [1] such as urea using the enzyme urease [1], cholera toxin (using its receptor) [11], carbofuran [12] and naphthalenic acid [13]. The lipid used in these detections was phosphatidylcholine.

The construction of graphene microelectrodes has been reported in the literature [1]. N-methyl-pyrrolidone (NMP) was mildly sonicated for 180 hours and centrifuged at 700 rpm for 2 h which provides a homogeneous dispersion ( $\sim 0.4 \text{ mg/mL}$ ). This dispersion was poured onto a copper wire (0.25 mm in diameter) which was placed on a glass microfiber filter and the solvent was evaporated. The copper acted as the connection for the electrochemical experiments.

The method of the construction of the lipid film nanobiosensors was reported in the literature [1]. The "receptor" molecules were inserted in these devices prior to polymerization by injecting 15  $\mu\text{L}$  of the "receptor" suspension on the polymerization mixture. The filter-supported polymeric BLMs were finally mounted onto the copper wire that contained the graphene nanosheets.

### References

1. Nikoleli GP, Israr MQ, Tzamtzis N, Nikolelis DP, Willander M, Psaroudakis N. Structural Characterization of Graphene Nanosheets for Miniaturization of Potentiometric Urea Lipid Film Based Biosensors. *Electroanalysis*. 2012;24(6):1285-95.
2. Tien HT, Salamon Z. Formation of self-assembled lipid bilayers on solid substrates. *J Electroanal Chem. Interfacial Electrochem*. 1989;276(3):211-8.
3. Christina GS, Dimitrios PN, Ulrich JK. A carbon dioxide biosensor based on hemoglobin incorporated in metal supported bilayer lipid membranes (BLMs): Investigations for enhancement of response characteristics by using platelet-activating factor. *Electroanalysis*. 1997;9(14):1043-8.
4. Nikolelis DP, Siontorou CG. Ammonium ion minisensors form self-assembled bilayer lipid membranes using gramicidin as an ionophore. Modulation of ammonium selectivity by platelet-activating factor. *Anal Chem*. 1996;68(10):1735-41.
5. Siontorou CG, Nikolelis DP, Krull UJ, Chiang KL. A Triazine Herbicide Minisensor Based on Surface-Stabilized Bilayer Lipid Membranes. *Anal Chem*. 1997;69(15):3109-14.
6. Andreou VG, Nikolelis DP. Flow injection monitoring of aflatoxin M1 in milk and milk preparations using filter-supported bilayer lipid membranes. *Anal Chem*. 1998;70(11):2366-71.
7. Dimitrios PN, Christina GS, Vangelis GA, Ulrich JK. Stabilized bilayer lipid membranes for flow-through experiments. *Electroanalysis*. 1995;7(6):531-6.
8. Nikolelis DP, Mitrokotsa M. Stabilized lipid film based biosensor for atenolol. *Biosens Bioelectron*. 2002;17(6-7):565-72.
9. Dimitrios PN, Garyfallia R, Georgia PN, Maria S. Stabilized Lipid Membrane Based Biosensors with Incorporated Enzyme for Repetitive Uses. *Electroanalysis*. 2006;18(24):2467-74.
10. Nikolelis DP, Raftopoulou G, Chatzigeorgiou P, Nikoleli GP, Viras K. Optical portable biosensors based on stabilized lipid membrane for the rapid detection of doping materials in human urine. *Sens Actuators B Chem*. 2008;130(2):577-82.
11. Stephanos K, Georgia PN, Christina GS, Dimitrios PN, Nikolaos T, Nikolas P. Development of an Electrochemical Biosensor for the Rapid Detection of Cholera Toxin Based on Air Stable Lipid Films with Incorporated Ganglioside GM1 Using Graphene Electrodes. *Electroanalysis*. 2016;28(7):1584-90.
12. Bratakou S, Nikoleli GP, Nikolelis DP, Psaroudakis N. Development of a Potentiometric Chemical Sensor for the Rapid Detection of Carbofuran Based on Air Stable Lipid Films with Incorporated Calix[4]arene Phosphoryl Receptor Using Graphene Electrodes. *Electroanalysis*. 2015;27(11):2608-13.
13. Bratakou S, Nikoleli GP, Siontorou CG, Karapetis S, Nikolelis DP, Tzamtzis N. Electrochemical Biosensor for Naphthalene Acetic Acid in Fruits and Vegetables Based on Lipid Films with Incorporated Auxin-binding Protein Receptor Using Graphene Electrodes. *Electroanalysis*. 2016;28(9):2171-7.