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SOME OPTIMIZATIONS OF BIO-FETs WITH ELECTRICAL CHARGED BIOLIQUID

C. RAVARIU[1], F. RAVARIU[2]

[1] *"Politehnica" University of Bucharest – Faculty of Electronics and Telecommunications 313, Splaiul Independentei, 77206, Bucharest, Romania, cristir@mcma.pub.ro*
[2] *Institute of Microtechnology, Bucharest, Romania*

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Abstract. The Bio-FETs are achieved with a matrix of receptor-analyte, coupled with an MOS Field Effect Transistor. The analytes could be antigens, proteins, hormons. The analytes binding provides a bias for the MOSFET transistor, but small enough. In this paper an optimisation is proposed of Bio-FETs that accumulate electric charge in the gate space, in order to increase the gate voltage with the same analyte concentration. This is possible by finding an optimum place for the receptor layer.

Key words: Biosensors, Field Effects Transistors, sensitivity optimisations, analytical methods.

INTRODUCTION

There are different methods for biosubstances detection. The convergence of biomaterials and microelectronic technologies has developed biodevices like ISFET [1, 2], ENFET [3], IMmuno-FET [4] or Microbial-FET, [5]. All these biosensors have the same transducer element – a Filed Effect Transistor, but different receptor types – Ion Sensitive Electrodes, ENzimes, Antigens, Microorganisms and belong to the class of Bio-FETs [6]. The receptors are quite distinct. The Ions Sensitive receptors are special metals: Pd, Pt, Ir. The ENzime layer immobilised in the gate of a MOSFET increases the enzymatic reaction rate in the gate space, emphasising a specific analyte. The immunosensors have an antibody (Ab) layer as biological recognition element. These are proteins, based on the principle "lock-key", that are binding only a specific foreign substance, called antigen (Ag). The antigen layer deposition onto the gate of a Field Effect Transistor (FET), opened the way toward IMmuno-FETs. M. Eray reported an immunosensor for acetylcholine with nicotinic acetylcholine receptors (nAChRs) [4]. Normally, acetylcholinesterase (AcChe) hydrolises acetylcholine, given H^+. Consequently it is not necessary to measure the acetylcholine concentration. The reaction products

H^+, are more comfortable to be detected by the potentiometric method, considering the H^+ ions as analytes [5].

Starting from this example, this paper analytically studies a MOSFET transistor with ionic analytes solved in a bioliquid, that is handled in the gate space. The analytes binding to the receptor layer increases the electric charge in the gate space, but small enough. An optimisation is proposed for this kind of Bio-FET in order to obtain a maximum gate voltage for the same analyte concentration. This is possible by finding an optimum place for the receptor layer.

THE BIO-FET STRUCTURE DESCRIPTION

A Bio-FET structure, that allows the bioliquid transport through the gate space, is shown in Fig. 1. The bioliquid is electrically charged with ions of analytes. The liquid transport, in the gate gap of MOSFET, could be achieved with a micro pump [7]. The gate gap could be manufactured with an Extended Gate (EGFET) technique [3] or with a Suspended Gate (SGFET) technique [8]. These assertions are not the target of this paper, but they prove that the nowadays technologies allow the Bio-FET fabrication. In this way the bioliquid is periodically circulated in the gate space via this gap.

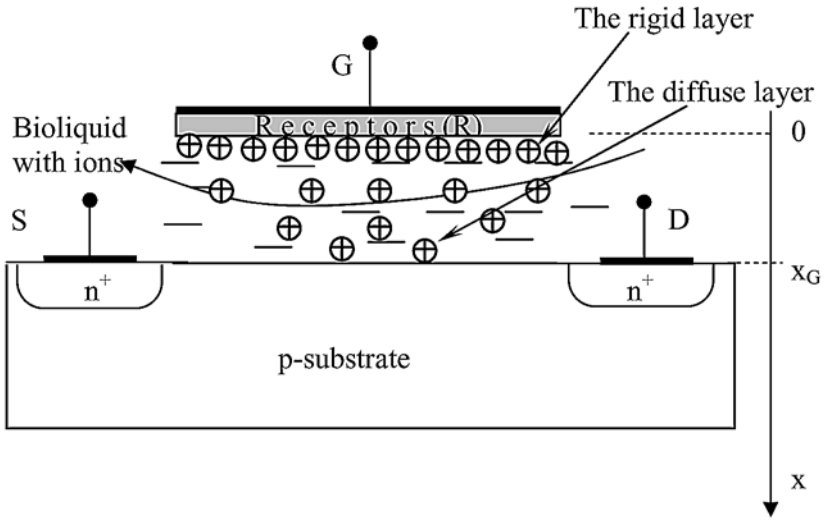

Fig. 1 – The Bio-FET structure represented with analytes coupled at the upper part.

The receptor layer could be entrapped near the gate metal – in the upper part – corresponding to Fig. 1 and Fig. 2a, near the semiconductor surface corresponding to Fig. 2b, or could be uniformly distributed in the gap space corresponding to

Fig. 2c. Consequently, the analytes are crowding near the receptor layer. Their electric charge biases the transistor. The spatial arrangement of ions near an electrode consists in the rigid and the diffuse layer forming [9]. The problem is to find the optimum place for the receptors in order to obtain the maximum gate excitation for the same quantity of analytes. An analysis from the electrical point of view is presented in the following paragraph.

3. THE ANALYTICAL MODEL

The analytes were associated with mobile ions in the bioliquid, noted by A^+, with a given concentration, c_A, given in molecules/cm^3. Three possible situations are shown in Fig. 2, according to the receptors position.

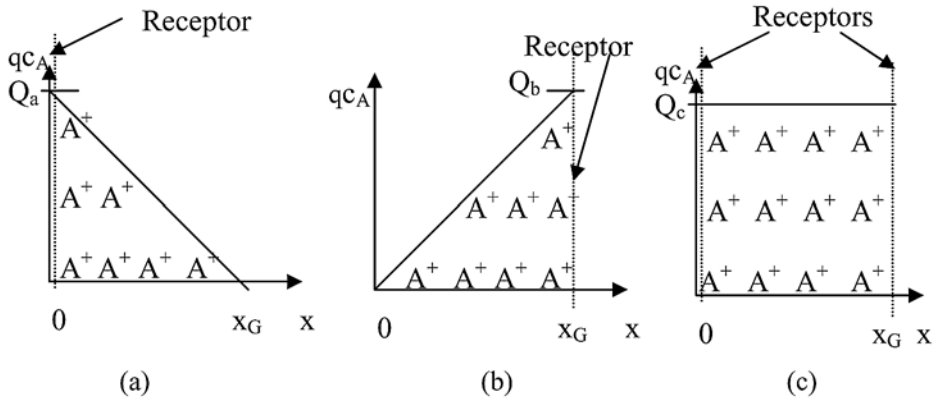

Fig. 2 – The analyte distribution, A^+ in the gate space, when the receptors were placed: (a) near the gate metal, (b) near the semiconductor surface, (c) uniformly distributed in the gap.

For all these distributions (Fig. 2a–c), a linear profile of the positive electric charge of the analyte was assumed. For a negative charged analytes, the gate bias can be optimised in a similar manner, but for an n-type semiconductor substrate. In case (a), the receptors trapped analytes in the upper space of the gate, Fig. 1. Consequently, the electric charge distribution looks like in Fig. 2a. These positive electric charges induce in the semiconductor an opposite sign charge. This is equivalent with the gate biasing. The analyte concentration, $c_A(x)$, is given by the equation of a straight line, crossing through 2 points. In case (a) it is:

$$qc_A(x) = -\frac{Q_a}{x_G} \cdot x + Q_a \quad \text{for} \quad x \in (0, x_G) \tag{1}$$

In case (b), when the analytes ions were crowding at the semiconductor surface (Fig. 2b), the electric charge density is:

$$qc_A(x) = \frac{Q_b}{x_G} \cdot x \quad \text{for} \quad x \in (0, x_G) \tag{2}$$

In case (c), when the analytes were dispersed in the entire volume of the gate gap, the electric charge density is:

$$qc_A(x) = Q_c = const. \quad \text{for} \quad x \in (0, x_G) \tag{3}$$

where $q = 1{,}6 \cdot 10^{-19}$ C is the elementary electric charge, c_A is the bulk analyte concentration in cm^{-3}, x_G is the gate gap width, x is the distance, Q_a, Q_b, Q_c represent the maximum of the superficial electric charge density encountered in the case a, b or c. The Poisson equation can be written:

$$\frac{d^2V}{dx^2} = -\frac{qc_A(x)}{\varepsilon_{bioliquid}} \tag{4}$$

By Poisson's equation integration, in cases (a), (b) and (c) the induced gate voltage, V_{Ga}, V_{Gb}, V_{Gc}, respectively, result:

$$V_{Ga} = \frac{1}{6} \cdot \frac{Q_a}{C_G} \tag{5}$$

$$V_{Gb} = \frac{1}{3} \cdot \frac{Q_b}{C_G} \tag{6}$$

$$V_{Gc} = \frac{Q_c}{C_G} \tag{7}$$

where C_G is the specific capacitance of the Bio-FET, $C_G = \varepsilon_{bioliquid}/x_G$, $\varepsilon_{bioliquid}$ is the electrical permittivity of the bioliquid. It is normal to study the case with the same quantity of analytes, so that the correlation relationship between Q_a, Q_b, Q_c charges is:

$$\int_0^{x_G} c_A(x)dx = \text{const. in case } a, b, c \quad \Rightarrow \quad Q_a = Q_b = 2Q_c \overset{not}{=} C_A \tag{8}$$

A higher gate voltage commands a higher drain current. Supposing that the entire quantity of analyte trapped in the gate gap is the same for all three cases, the best response is given by that sensor that provides a maximum gate voltage. Hence, a maximum sensitivity yields in the case (c), according to the result (7).

In Table 1 are presented some results of the analytical model, for a Bio-FET with different C_A and x_G parameters, for $\varepsilon_{bioliquid} = 7 \cdot 10^{-12}$ F/cm.

The maximum gate voltage is obtained in the case c. It is obvious from Table 1 that the maximum response yields for a higher gate space and for a higher

Table 1

The equivalent gate voltages induced by an analyte in Bio-FET with the receptor layer deposited: (a) near the gate metal, (b) near the semiconductor surface, (c) uniformly distributed in the gap

Conditions	V_{Ga} (V)	V_{Gb} (V)	V_{Gc} (V)
$C_A = 1\times10^{11}$ ecm^{-2}, $x_G = 1$ μm	0.037	0.075	0.113
$C_A = 1\times10^{12}$ ecm^{-2}, $x_G = 1$ μm	0.378	0.757	1.136
$C_A = 1\times10^{13}$ ecm^{-2}, $x_G = 1$ μm	3.787	7.575	11.363
$C_A = 1\times10^{12}$ ecm^{-2}, $x_G = 5$ μm	1.893	3.787	5.681
$C_A = 1\times10^{12}$ cm^{-2}, $x_G = 0.5$ μm	0.189	0.378	0.568
$C_A = 1\times10^{12}$ cm^{-2}, $x_G = 0.1$ μm	0.003	0.007	0.011

electric charge concentration, in a given situation for the receptor place. An electric charge concentration about $C_A = 10^{12}$ ecm^{-2} means a number of molecules about 10^{16} molecules of analyte/cm^3, that means a molar concentration of analyte in the range $C_v = 0.01$ μmol/ml. The detection of this low analyte concentration is useful in IMuno-FETs, [6].

4. SOME PRACTICAL EXAMPLES

Several authors investigated the Bio-FETs incorporating the enzyme receptor in the gate space. For example, glucose-oxidase (GOD) catalyses the glucose oxidation. In MOSFET technology, the enzyme receptors are both physically entrapped in polyacrymide on nylon netting and chemically bounded to polyacrylic acid derivatives [2, 6].

An enzymatic method for urea determination is based on the urea hydrolysis in urease enzyme presence. Thus, not the organic compound is measured. The reaction products are more easy to be detected as ionic analytes, according to:

$$(NH_2)_2CO + 3H_2O \overset{urease}{\rightarrow} 2NH_4^- + OH^- + HCO_3^-$$

The Bio-FET was accomplished with some Ion Selective Electrodes Ir/Pd deposited on the gate oxid of a MOSFET. The urea concentration was read in the range 1…300 μmol/l, monitoring the positive ions of NH_4^+, [2]. In this case the receptor layer is placed on to the gate oxide, over the gate. This biodevice has no gap in the gate space for bioliquid handling, but can be regarded as a Bio-FET in case (a). Knowing the urea molar mass, M = 60 g/mol, the ionic analyte concentration varied in the range 6×10^{14}…1.8×10^{17} cm^{-3}. For $x_G = 0.5$ μm a variation for C_A resulted in the range 3×10^{10} ecm^{-2}…5×10^{12} ecm^{-2}. According the model (5) the gate voltage varied by 0.0056 V…0.946 V, according to experimental results [2].

5. CONCLUSIONS

In this paper was presented an analytical model that controls the dependence analyte concentration, c_A *versus* the induced gate voltage, V_G. This is a starting point for future biosensors modeling. The analytical model is based on the integration of Poisson's equation. The results show that the optimum occurs when the receptor layer is uniformly distributed in the gap. If this target is not technologically possible, the following optimum solution is the receptors entrapping near the semiconductor surface. In this way, the gate voltage increases three times *versus* the case of receptors entrapping near the gate metal. If the receptors are entrapped both near the gate electrode and the semiconductor surface, that is roughly equivalent with a uniform distribution of the receptors in the gap, the gate voltage increases six times.

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