Beyond the Debye length: Direct protein detection in human serum with FETs and a portable biomedical system

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Abstract

Field-effect transistors (FETs) have been extensively used for biosensors due to their high sensitivity and label-free detection. However, conventional FET-based biosensors suffer from the charge screening effect in high ionic strength solution, leading to lower sensitivity. It turns out that most FET-based biosensors detect proteins in diluted solution, and complicated washing processes are usually needed. In this study, a new type of field-effect transistors, which are different from conventional FETs, are demonstrated to be able to detect proteins in high ionic strength solution, as similar as in human serum. By using the new method, we have also developed a portable measurement system using FET biosensors for home healthcare.

1. Introduction

Field-effect transistors (FETs) have been widely used for biosensors due to their high sensitivity and small size. FET-based biosensors have been demonstrated with many different materials, such as Si [1], carbon-nano tube [2] or graphene oxide [3]. Most of them are used as conventional FET-based biosensors, in which the gate region between source and drain was immobilized with receptors, such as antibody or DNA aptamers, as shown as in Figure 1. The binding between the analyte (antigen) and receptor (antibody), causing the surface potential change on gate region above the channel, leading to the change of carrier concentration in the channel of FETs, resulting in the conductivity change. Nano-wire FETs have been also studied and shown very high sensitivity. However, These conventional FET-based biosensors face an intrinsic problem, the charge screening effect in high ionic strength solution. In human blood or serum, the ionic strength is close to 1XPBS (phosphate buffer solution), which is quite high and leads to a quite small Debye length (~0.7nm), as shown in Figure 1. The Debye length in buffer solutions with different salt concentrations are 0.7nm, 2.4nm, and 7.4nm, respectively. It is obvious that the Debye length in 1XPBS is much shorter than the size of a regular antibody, which is 3~5nm [1]. The surface potential change caused by the antigen, will be mostly screened off, leading to the difficulty to detect protein in physiological environment [4-5].

![Debye length in buffer solutions with different salt concentration.](image)

Fig. 1 The Debye length in buffer solutions with different salt concentration.

Electric-double-layer transistors (EDLTs) were reported previously [6-8], using electrolyte or ionic liquids as the gate dielectric. The ionic liquid, for example, can easily generate much higher charge density compared to regular dielectric, such as SiO₂, resulting in larger change in carrier concentration in the channel, thus improving the device performance [6-8]. In this study, EDLTs are used to detect protein in physiological environment. The results show that EDLTs are promising in detecting proteins in high ionic strength solution, which will be able to solve the problem from the charge screening effect for FET-based biosensors, making FETs become much simpler to use for point-of-care or homecare devices.

2. Experimental and Results

Fabrication of AlGaN/GaN high electron mobility transistors (HEMTs) sensors

The AlGaN/GaN epi wafer was grown on a silicon substrate. The multilayer structure starts with a 3 μm-thick undoped GaN buffer layer, 250 Å-thick undoped Al0.25Ga0.75N layer and 30 Å-thick undoped GaN cap layer. The epilayers were grown by metal-organic chemical vapor deposition (MOCVD). The two-dimensional electron gas at the interface between AlGaN and GaN layer was formed. The AlGaN/GaN HEMTs was processed with photolithography with Aligner. Mesa layer was first developed and followed by an Inductively Coupled Plasma (ICP) etching system with Cl2/BCl3 gases under ICP power of 300 W at 2 MHz. After mesa etching, the source/drain metal was fabricated...
formed as Ohmic contacts. The Ohmic contacts separated with gaps of 30 µm consisted of e-beam deposited Ti/Al/Ni/Au and was annealed at 850 °C, 45 sec under flowing N2. After finishing Ohmic contacts, the final metal (Ti/Au) was formed with photolithography, followed by metal deposition with an evaporator, and then the lift-off process was done. The final metal was used for connecting the source/drain for further electrical measurement. Finally, photoresist was coated and only the gate electrode and the active channel region between source and drain were opened. Antibody or DNA aptamer were immobilized on the transistors. The sensors were then tested in 1XPBS and in serum for protein detection. The topview of the sensor is shown as in Fig. 2.

Fig. 2 Photography of the topview of the AlGaN/GaN HEMT.

FET biosensor package and the portable measurement system

A miniaturized FET biosensor was packaged with a microfluidic channel. The whole size of the packaged biochip is the same as a commercial micro SD card, as shown in Fig. 3(left). The micro SD card was able to insert into the socket, which connects to a portable measurement system, as shown in Fig.3(right). The whole system is connected to a laptop and a software is able to control the measurement system, as shown in Fig. 4. This whole system has been demonstrated for direct human serum detection with 5 minutes, without washing process.

Fig. 3(left) The packaged FET-biosensor with microfluidic channel. (right) The packaged biochip inserted into a micro SD card socket.

3. Conclusions

In this study, we have demonstrated a new methodology for measuring field-effect-transistor (FET)-based biosensors in high ionic solution. The new methodology uses EDLTs and allows the transistors to detect proteins in physiological salt concentrations with high sensitivity. This technology shows the promising applications of FET-based biosensors with less process and instrument required, providing fast and simple detection, which is suitable for point-of-care or personal healthcare monitoring. Finally, a packaged FET biosensor and a whole portable measurement is also developed and demonstrated with good functions.

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