

Recording of living cell membrane depolarisation with AlGaIn/GaN sensor

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Abstract:

This work reports on AlGaIn/GaN-based sensor development and application to biological sensing. Living cells were seeded on the sensitive region of encapsulated devices for 30 minutes before membrane depolarisation with KCl. To confirm cell activity KCl was also added to devices in physiological salt solution with no cells. The resulting responses were recorded in both cases and demonstrated significant differences in profile and amplitude. Since the AlGaIn/GaN structure itself is ion-sensitive, a chemical signal is expected even in the absence of cells. The depolarisation signal observed for the devices with cells is thus expected to incorporate this chemical response.

Key words: AlGaIn/GaN, sensors, biological sensing, living cells based sensing.

Introduction

AlGaIn/GaN sensor technology is a successor to silicon based field effect transistor (FET) based sensors, with higher chemical stability in liquids and better compatibility with living cells [1]. Therefore AlGaIn/GaN heterostructures are promising for the development of biochemical sensors employing extracellular signal recording. In the last decade AlGaIn/GaN sensors have been demonstrated for recording of cell action potential, non-invasive cell electrophysiological measurements and electrical stimulation of cell culture. However, the strength of the recorded signal was often only in the range of tens to hundreds of micro volts [2-4]. In this study we demonstrate a high amplitude (milli volts) signal during stimulated membrane depolarisation of living cells via exposure to the KCl. The absence of this high amplitude signal in the control experiment confirmed that the signal corresponded to an extracellular event associated with the depolarisation.

Experimental Methods and Results

Ungated devices were fabricated on standard AlGaIn/GaN wafers with 2nm GaN capping layer. The measurements were performed on packaged four point bar structure devices with sensing areas of 1.25 x 0.5 mm, at constant current of 100 μ A using a DT82E DataTaker

and constant current source. All measurements were performed inside a custom-built environmental chamber under constant temperature (37°C) and constant light conditions. Standard cleaning was applied to the sensor surface (acetone, isopropyl alcohol, DI water and N₂blow-dry) after device fabrication and between measurements.

Human Coronary Artery Endothelial Cells (HCAEC) were cultured in MesoEndo Cell Growth Medium and re-suspended in standard physiological salt solution. Living cells in physiological salt solution (500 μ L) were seeded on the device sensitive area 30 minutes before depolarization, which allows cells to attach to the sensitive area of device. To achieve cell membrane depolarisation 45 mM of KCl was added to the cell medium and the resulting signal was recorded (repeated three times).

For the measurement configuration used here, exposure of the surface to charge, including ionic solutions, leads to a shift of the surface potential and thus to a change in the sheet carrier density of the two dimensional electron gas (2DEG) located at the AlGaIn/GaN interface. This change is directly recorded through a time dependent measurement of potential drop across the sensitive area for constant applied current.

To identify the nature of the observed signal a control experiment with physiological salt solution but no living cells was undertaken. The device sensitive area was exposed to 500 μL of physiological salt solution and 45 mM of KCl was added (repeated three times). The resulting signal demonstrated that the devices are, as expected, sensitive to changes in ionic concentration. However, the profile and

amplitude of the control experiment signal is substantially different from the signal when living cells are present. Both experimental results can be seen in Fig.1. Therefore we can state that the AlGaN/GaN sensors presented here are capable of recording biological signals, in particular living cell membrane depolarisation.

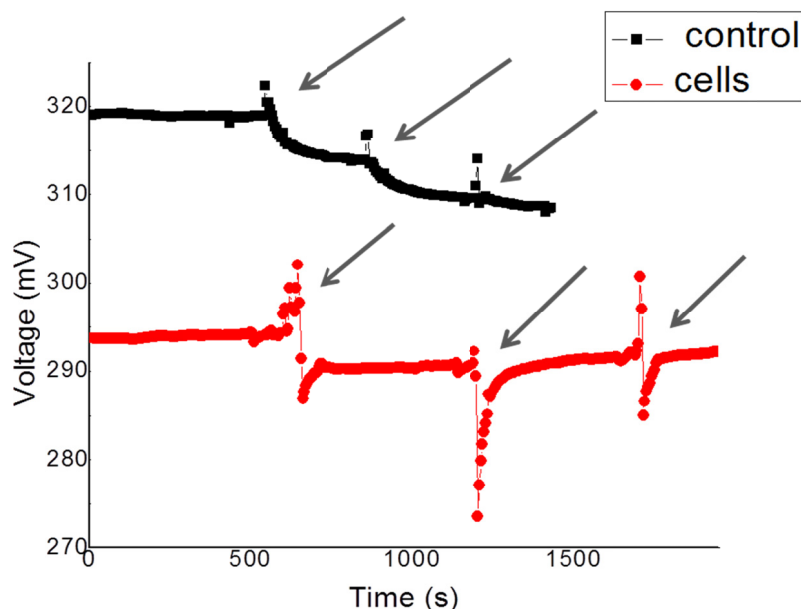


Fig. 1. Device responses to addition of 45 mM of KCl, for devices with cultured cells ("cells") and devices in physiological salt solution only ("control"). Data was obtained by making time dependent measurements of voltage across the sensitive area of device under constant current of 100 μA .

Conclusion

An AlGaN/GaN-based sensor has been demonstrated to show sensitivity to KCl and physiological salt solution both with and without the presence of living cells. However signals recorded with cells seeded on the sensitive area of packaged devices had higher amplitudes and different profiles and thus are considered to contain both chemical (ion concentration) and biological (cell depolarisation) components.

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