A novel detection of non-nucleoside reverse transcriptase inhibitors (NNRTIs) for HIV-1 with AlGaN/GaN high electron mobility transistors

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Since AIDS caused by HIV-1 (human immunodeficiency virus type 1) has been in the top 10 leading causes of death for many years, there have been many promising treatment discovered. One of the treatments is by taking non-nucleoside reverse transcriptase inhibitors (NNRTI) to suppress the activity of the HIV-1. The binding affinity of NNRTI to the reverse transcriptase (RT) of HIV-1 is an important factor determining the efficiency of the drug performance. The HIV-1 RT immobilized AlGaN/GaN high electron mobility transistors (HEMTs) were used to find the dissociation constant of NNRTI. Comparing to traditional drug analyzing, HEMTs assisting experiments are much faster in processing time and lower cost with high accurate results.

Figure 1 (a) and (b) show the schematic of RT immobilized HEMT and the top-view of the device respectively. The HEMT was constructed by a100Å-thick gold layer on the gate region, a 10 Å-thick undoped GaN cap layer, a 150 Å-thick undoped $Al_{0.25}Ga_{0.75}N$ and a 3 μm-thick undoped GaN buffer layer. The source and drain of HEMT were isolated by photoresist except the gate metal region. The RT were immobilized by using 6-Mercaptohexanoic acid as cross-linker on the gold surface. Figure 2 is the real time signal extracted from HEMT by dropping different concentration of NNRTI at a constant 0.5 V bias of HEMT. At the beginning, pure buffer were dropped on the gate until there was no current change. And then buffer with different final concentrations of NNRTI from 10 pM to 2.9 uM were doped sequentially. At the end, the current went saturated without any change induced by different concentrations.

The dissociation constant of NNRTI was analyzed by using Langmuir isotherm equation:

$$[NNRTI]/\Delta I=[NNRTI]/\Delta I_{max}+K_D/\Delta I_{max}$$

ΔI is the current change at each different concentrations and ΔI_{max} is the current change at saturated concentrations. The surface coverage ratio α was found by rearranging the equation above:

$$\alpha=\Delta I/\Delta I_{max}=1/(1+K_D/[NNRTI])$$

In Figure3 shows the fitting result of α. It represents the amount of NNRTI binding with the RT at each concentration. The K_D extracted from the analysis is 0.193 nM and R^2 is 0.9990. It also shows good sensitivity from 10 pM to 10 nM.

To summarize, the RT immobilized HEMT analyzing the K_D of NNRTI is a very powerful tool in the future to develop new type of NNRTIs. Considering its low time consuming and high accuracy results, the drug efficiency can be predicted at the early stage. It can save lots of effort to develop the new drugs by identifying the K_D, and only the drugs with good potential need to be furthermore tested.

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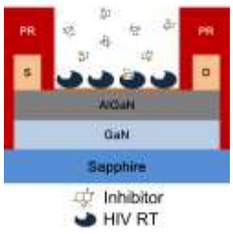

(a)

(b)

Figure 1.(a) The schematic of RT immobilized HEMT. (b) The top-view of the HEMT.

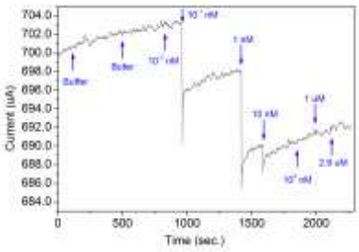

Figure 2. The Real time signal extracted from HEMT.

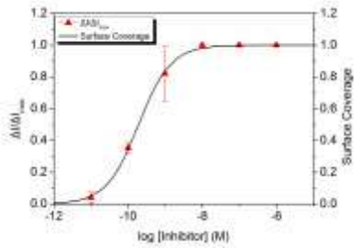

Figure 3. Surface coverage ratio from rearranged Langmuir isotherm equation.