Limit of detection of field effect transistor biosensors: Effects of surface modification and size dependence

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Field-effect transistor biosensors have shown great promise in the detection of biomolecules. However, a quantitative understanding of what limits the smallest measurable concentration of analyte (limit of detection or LOD) is still missing. By considering the signal-to-noise ratio (SNR), extracted from a combination of noise and I-V characterization, we are able to accurately predict and experimentally confirm a LOD of 0.01 pH. Our results also show that devices with larger area and with amine functionalized surfaces have larger SNR. We are able to extract the associated oxide trap densities and, thus, quantify the improvements in LOD.

Noise analysis is a tool that has only recently been adopted by the nanowire research community1–4 and only more recently been applied to the field nanowire/nanoribbon based biosensors.5–7 A commonly used metric in the field of biosensors is the sensitivity, defined as the relative change in the signal (ΔI/I), which allows for comparisons across devices with different dimensions and transfer characteristics. Consequently, a lot of theoretical as well as experimental conclusions are based on the optimization of this performance metric.8,9 However, as far as the limit of detection (LOD) of sensors is concerned, this metric fails to account for the primary limitation which is the noise of the particular sensor system/device. As devices are scaled down to the nanometer regime, the channel current becomes more prone to fluctuations due to oxide traps and interface states and the low-frequency noise of the device becomes a very serious limitation for any DC measurement.10,11 Noise can also originate from the interactions at the dielectric/solution interface.12 In the case of our field effect transistor biosensors (bioFETs), the channel noise dominates,5 and we consider semiconductor 1/f noise only. Therefore, it becomes essential, in the design of “better” sensors to consider a performance metric, which includes the effects of noise fluctuations, as well as, provides a physical model to understand the parameters which affect the LOD. Signal-to-noise ratio (SNR) can be used as such a metric,13,14 since it involves both the device transconductance (g_m) which is directly proportional to the signal generated, as well as the current noise power density (S_I), which is a function of device dimensions as well as oxide trap density (N_{ox}).15 The SNR for bioFET devices has been defined earlier14 and to summarize, using the number fluctuation model,16 it can also be presented in this form

\[
SNR = \frac{g_m}{\sqrt{S_I}} = \frac{1}{\sqrt{S_{VFB}}} = \frac{WLC_{ox}^2f}{\lambda kT q^2 N_{ox}} \sqrt{\frac{f}{f}}.
\]  

(1)

SNR here is defined per unit change of surface potential and per unit “bandwidth,” BW defined as BW = ln(f_2/f_1). W and L are the widths and lengths of the device, respectively, \(\lambda\) is the tunneling parameter for electrons in silicon oxide (\(~10^{-10}\) m), k is the Boltzmann constant, T is the temperature, f is the frequency at which the power of the noise density is measured, and C_{ox} is the oxide capacitance per unit area. N_{ox} is the oxide trap density, and in the case of ultra-scaled devices, it includes contributions due to surface states and interface traps/defects.17,18 It follows that the minimum detectable surface potential change (the limit of detection assumed at a measured signal-to-noise ratio of 1) is given by 1/SNR, which is limited by the flat-band voltage fluctuations due to the effects of traps and interface states. SNR can be easily determined by a combination of noise measurements and I_{d}-V_{g} characterization and, consequently, used to either compare devices with different LOD or screen the devices with the lowest LOD, prior to a biosensing experiment.

Silicon nanoribbon devices (effective widths ranging from 1 to 100 µm) are fabricated from “4” (100) Silicon-on-Insulator wafers (SOITEC Inc.) with a 50 nm of active p-doped Si layer (resistivity 1–10 Ω-cm) and 145 nm of buried oxide (BOX) layer. To improve the reliability and lifetime of the sensors when exposed to an electrolyte environment, a 15–20 nm top-oxide (TOX) was grown using dry O_2 oxidation in a tube furnace at 1100°C. To isolate the metal leads from the solution during sensing experiments and to ensure that only the device region is directly in contact with the aqueous environment, a 2 µm thick SU-8 layer was deposited, patterned, and subsequently hard-baked at 150°C. We have previously shown that the SNR is bias-dependent and, therefore, can be optimized by choosing the proper gate voltage.14 Figure 1(a) shows the noise characterization, as well as, transconductance curve of a bioFET device with a peak SNR of approximately 11 000, which is maximized close to the region of peak transconductance. The peak SNR value of 11 000 translates to a minimum detectable voltage of ~270 µV (for a typical sensing measurement, sampling rate is around 10 Hz, and the measurement takes about 30 min,19 which gives \(~BW \sim 3\), and, with an
extracted pH sensitivity of 23 mV/pH for that device (not shown here), we deduce a limit of detection in terms of pH of 0.01. The pH sensitivity of the device varies with the quality of the surface modification and is usually found to be in the range of 20–50 mV/pH. Figure 1(b) shows a successful detection of a pH change of 0.07 with a signal-to-noise ratio of ~3.5. This results in a measured LOD of 0.02 pH, which agrees well with the theoretical LOD derived above. This shows that we can use the SNR defined in Eq. (1) as a reliable and quantitative way to predict the performance of a bioFET sensor, before the actual sensing experiment and before extensive and time consuming biofunctionalization steps. More importantly, understanding what affects the SNR from the device standpoint and how to optimize it, would ultimately lead to the design of sensors with lower limits of detection.

The effect of surface functionalization on device performance and noise, separately, has been reported. However, the effect of the surface passivation/functionalization has not been studied in the context of the SNR. Considerations of noise and device parameters, such as mobility and subthreshold slope, separately, are not very useful in predicting the limit of detection of the bioFET sensor. Moreover, the effect of (3-aminopropyl)triethoxysilane (APTES) functionalization on the noise properties has not been previously studied. APTES functionalization is a common first step to bio-molecular functionalization of a bioFET sensor surface as well as being a widely used pH sensitive layer, known to improve the pH sensitivity of silicon oxide surfaces. Figure 2(a) shows the normalized current noise power density plotted as a function of drain current for two sets of devices, of exactly the same dimensions, but one set functionalized with APTES while the top oxide of the other set of devices remained un-functionalized (bare oxide devices). The results indicate that functionalization with APTES results in reduced current fluctuations which is most likely due to the passivation of surface states, which effectively reduces $N_a$ in Eq. (1). It is important to note that $N_a$ refers to an effective trap density which includes the effects of traps located at the semiconductor/oxide or in the oxide, close to that interface. In the case of bioFETs, there are two interfaces that can cause the gate voltage to fluctuate, namely the silicon/oxide interface and the oxide/electrolyte interface. The exact mechanism is not fully understood, but it would seem that APTES functionalization suppresses the charge interactions at the oxide/electrolyte interface, resulting in a lower effective trap density as measured in the device drain current. The reduction is more significant in the subthreshold regime (upto 60 $\times$ lower) than in the linear regime, which is the optimal operating regime for better SNR.

FIG. 1. (a) Plot of the SNR and the device transconductance ($g_{md}$) as a function of solution gate voltage, highlighting the observation that SNR is maximum at the point of peak transconductance. The maximum SNR for this device is 11 000, which translates to a minimum detectable pH change of 0.01. (b) pH sensing experiment to investigate the LOD of the bioFET sensor, showing the detection of a change in 0.07 pH with a measured signal-to-noise ratio of ~3.5.

FIG. 2. (a) Comparison of the normalized current noise power as a function of drain current, for APTES functionalized devices vs. un-functionalized bioFETs (bare oxide surface). The APTES functionalization results in a significant reduction in the current noise power density. (b) The extracted SNR compared for the functionalized and bare oxide devices, showing the improvement that results from bioFET surfaces chemically modified with APTES.
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Figure 2(b) shows the peak SNR that was extracted from the same sets of devices, clearly demonstrating the improved signal-to-noise ratio that accompanies the reduction in current noise power density. The APTES functionalized devices, on average, show an increase of about 3-fold in the SNR which represents almost an order of magnitude decrease in the trap density, for the surface modified bioFETs, and highlights both the impact of surface states on the measured device characteristics for nano-scale thickness devices as well the possibility of modifying/reducing these surface states by chemical modification of the dielectric surface. The extracted trap densities for the APTES functionalized and bare oxide devices were $2.7 \times 10^{-17} \text{eV}^{-1}\text{cm}^{-3}$ and $2.4 \times 10^{-18} \text{eV}^{-1}\text{cm}^{-3}$, respectively.

The current signal generated by a sensor ($\Delta I$), for a particular change in surface potential, is directly proportional to the transconductance ($g_m$) which is given by

$$g_m = \frac{W}{L} \mu C_{ox} V_{DS},$$  \hspace{1cm} (2)

where $\mu$ is the effective mobility of charge carriers and $V_{DS}$ is the drain-to-source voltage, which is kept constant at 0.1 V for all noise measurements. Figure 3(a) shows the linear dependence of $g_m$ on the ratio $W/L$, verifying that Eq. (2) holds for the devices used in this work. The transconductance was extracted by numerical differentiation of the $I_D-V_G$ curve, and the peak $g_m$ values were recorded and subsequently plotted. The SNR is defined as the ratio of $g_m$ and the drain current noise amplitude given by $\sqrt{\langle I^2 \rangle}$ (f = 1 Hz). Therefore, it is important to de-couple the effects of transconductance and noise. Re-casting the SNR in terms of voltage fluctuations, such as in Eq. (1), gets rid of the dependence on $g_m$ and allows us to focus on what truly limits the minimum detectable voltage, namely, the gate-voltage referred noise ($S_{V_{FB}}$). Equation (1) predicts that the SNR is directly proportional to the square root of the device area. The devices measured were all from the same wafer, with a silicon oxide top-gate dielectric of thickness 20 nm, resulting in a constant $C_{ox}$ for all measured devices. Figure 3(b) indeed shows a linear relationship between SNR and $\sqrt{(WL)}$, validating the use of Eq. (1) in better understanding and engineering devices with lower limits of detection. The data also demonstrates that increasing the device area results in larger SNR and therefore more sensitive bioFET sensors, which is in direct contrast with the common scaling argument that smaller devices result in larger relative signal change and, therefore, will behave as more sensitive biosensors. The use of the relative signal change ($\Delta I/I$) as a metric has the fundamental limitation that it does not consider how the noise also scales with device dimensions. Here, we need to point out that the SNR scales with $\sqrt{(area)}$ in so far as the surface potential changes over a constant proportion of the whole device area. This is generally true for pH sensing experiments, where the surface potential changes over the whole device area. The situation can be very different when considering low numbers of analyte molecules and a much larger binding affinity, for which, the percent surface coverage is reduced as the area is increased, since the number of available molecules is not enough to bind to the available receptors, and hence, the surface area of the device must be optimized. If such optimization is not carried out, the signal will be derived from an area much smaller than the device area, whereas the noise will still be generated from the whole device area, resulting in a degradation of the signal-to-noise ratio.

A common amplification strategy for dual-gated biosensors is to measure the back-gate response due to a surface potential change at the top-gate. The ratio of the capacitance of the top-gate to that of the back-gate ($C_{TC}/C_{BG}$) provides the voltage amplification. In our devices, this ratio is roughly equal to 6, as can be seen from Table I, and the ratio of $g_m$ was measured to be about 5 for the two gating schemes applied to the same set of devices ($W = 2 \mu m$ and $L = 10 \mu m$). Table I also clearly shows that the SNR is degraded when the back-gating scheme is employed. The SNR is reduced by a factor of ~10, which cannot be solely explained by the smaller capacitance of the back gate (factor of ~5), which would only result in a 5-fold reduction in SNR. We believe that the additional reduction in SNR is due to the different oxide trap densities involved when the top-gate oxide is used as opposed to the back-gate oxide. The back-gate oxide is the BOX from the Smart-Cut process, whereas the top-gate oxide is formed from the dry oxidation of the active silicon layer. The BOX has a slightly higher oxide trap density (~4× higher) which results in the...
Additional reduction in SNR when the measurement is carried out using the back-gate. We calculated the oxide trap densities involved in each gating scheme, and the results are presented in Table I. Even though measuring using the back-gate yields a larger voltage change due to the smaller capacitance, any fluctuation in the BOX charge will also couple to the channel and produce larger voltage fluctuations. Thus, voltage amplification using the back-gate is canceled out by an equivalent voltage noise increase (Even though SNR as defined in Eq. (1) decreases, it is defined per unit voltage change in surface potential and therefore, does not factor in the voltage amplification. The measured signal-to-noise ratio remains the same with or without amplification). However, if the BOX has a higher trap density than the TOX, such as in the case of our devices, the voltage noise increases by a larger amount than the amplification of the signal, and back-gated measurements consequently become less sensitive than top-gated ones.

Using SNR as a performance metric allows us to accurately place a lower bound on the limit of detection of a bioFET device in an actual sensing experiment. Thus, this metric not only enables us to screen devices that have the desired sensitivity but also aids in the design of sensors with lower detection limits. The effect of APTES functionalization is quantified as almost a 3-fold enhancement in the SNR and, consequently, almost an order of magnitude decrease in the limit of detection for APTES functionalized surfaces compared to bare silicon oxide. SNR is also shown to increase as $\sqrt{\text{area}}$, which means that aggressive scaling is not always the best solution and that careful sizing of the device, based on the experimental requirements, is very important in order to optimize the SNR while keeping the device density high. The effect of oxide capacitance on the measured SNR is quantified, and we extract a trap density of $7.6 \times 10^{17} \text{eV}^{-1} \text{cm}^{-3}$ for the buried oxide as compared to a trap density of $2.1 \times 10^{17} \text{eV}^{-1} \text{cm}^{-3}$ for the top oxide. In this case, voltage amplification by back-gate measurements will result in lower measured SNR as compared to top-gated measurements, since the noise is amplified along with the signal, and the noise is intrinsically higher for the back-gate compared to the top-gated case (due to a larger $N_{\text{ox}}$ in the BOX).

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<table>
<thead>
<tr>
<th>Gating scheme</th>
<th>Oxide thickness, $T_{\text{ox}}$ (nm)</th>
<th>Avg. peak $g_m$ (nA/V)</th>
<th>Avg. peak SNR ($V^{-1}$)</th>
<th>Trap density $N_{\text{ox}}$ ($\text{eV}^{-1} \text{cm}^{-3}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solution gated</td>
<td>20</td>
<td>380</td>
<td>66 000</td>
<td>$2.1 \times 10^{17}$</td>
</tr>
<tr>
<td>Back-gated</td>
<td>80</td>
<td>120</td>
<td>6900</td>
<td>$7.6 \times 10^{17}$</td>
</tr>
</tbody>
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Table I. Comparison of the SNR measured using the back-gating scheme to the SNRs extracted from solution gated measurements. Equation (1) predicts a reduction in the SNR for the back-gated measurements due to the lower capacitance, and from the additional degradation in the SNR, we extract values for the oxide trap density ($N_{\text{ox}}$) of the buried oxide and the top gate oxide.