Metal-coated microfluidic channels: An approach to eliminate streaming potential effects in nano biosensors

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ABSTRACT

We report a method to suppress streaming potential using an Ag-coated microfluidic channel on a p-type silicon nanowire (SiNW) array measured by a multiplexed electrical readout. The metal layer sets a constant electrical potential along the microfluidic channel for a given reference electrode voltage regardless of the flow velocity. Without the Ag layer, the magnitude and sign of the surface potential change on the SiNW depends on the flow velocity, width of the microfluidic channel and the device's location inside the microfluidic channel with respect to the reference electrode. Noise analysis of the SiNW array with and without the Ag coating in the fluidic channel shows that noise frequency peaks, resulting from the operation of a piezoelectric micropump, are eliminated using the Ag layer with two reference electrodes located at inlet and outlet. This strategy presents a simple platform to eliminate the streaming potential and can become a powerful tool for nanoscale potentiometric biosensors.

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1. Introduction

In the past decade, nano-scale field effect transistor (FET)-based devices, such as Si nanowires (SiNW), Si nanoribbons, carbon nanotubes (CNT), graphene, and metal oxide nanowires (NW) have attracted significant attention in biological and chemical sensing, due their ability to achieve label-free, real-time detection at high sensitivity (Chen and Zhang, 2011; Cui et al., 2001; Guo et al., 2013; Smith et al., 2014; Stern et al., 2007a; Wipf et al., 2013, Zhang et al., 2011, 2015). In particular, silicon-based devices fabricated by top-down approaches have the advantage to be integrated with readout circuitry on-chip with high reproducibility for mass production at low cost (Lee et al., 2015, 2013; Livi et al., 2013; Luo et al., 2009; Mu et al., 2014; Rigante et al., 2015; Stern et al., 2007a; Zhang et al., 2010). They have shown their potential as promising biosensors to detect a wide range of charged biological species, such as DNAs and proteins with high sensitivity (Bunimovich et al., 2006; Duan et al., 2012). Real-time and label-free detection has been successfully demonstrated by detecting variations in the surface potential upon binding of charged analytes in the electric double layer at the sensor surface (Duan et al., 2012; Wipf et al., 2016).

The common strategy for label-free biosensing is to immobilize the receptors on the sensor surface. For the detection of large molecules such as proteins or DNA, the Debye length of the buffer solution needs to be considered to optimize the sensing performance, as the charges from the target molecules are screened outside of the electrical double layer (EDL) (Schaafort et al., 1990; Stern et al., 2007b; Vacic et al., 2011). This leads to a significant reduction in the sensor response. The Debye length is mainly affected by the ionic strength of the buffer solution. To extend the sensitive spatial boundary of the sensor, the ionic strength of the buffer solution can be reduced. This approach has been used in several biosensing applications (Chen et al., 2011; Duan et al., 2012; Mu et al., 2015; Stern et al., 2010; Zhang and Ning, 2012). However, reduced ionic strength can introduce additional noise as the stability of the solution's electrical potential is influenced by electrolytes with low conductivity. In particular, potentiometric biosensors using microfluidics and flow systems for analyte detection are affected by streaming potential (Kim et al., 2009). In reference (Wipf et al., 2016) microfluidic channels had little effect on the signal, but significantly increased the noise in protein detection measurements in low ionic strength buffer as compared to a larger fluidic system.

The EDL has a characteristic potential distribution given by the surface material, as well as the ionic composition and pH of the electrolyte. The Gouy-Chapman-Stern model is commonly used to describe the potential and charge distribution in EDLs (van Hal et al., 1996). In short, surface charges attract counter ions from the...
solution. The first immobile layer of counter ions, called the Stern layer, is followed by the diffuse layer as shown in Fig. 1. The Zeta potential ($\zeta$) is defined as the potential difference between the bulk electrolyte and the slipping plane that separates mobile fluid from fluid that remains attached to the surface. The streaming potential ($V_{str}$) in a microfluidic channel is generated in the EDL of a pressure driven flow (Kirby and Hasselbrink, 2004; Mansouri et al., 2005; Vanwagenen and Andrade 1980). The flowing solution carries excess counterions in the diffuse layer downstream, which leads to a longitudinal electric field along the flow direction. $V_{str}$ is defined as the potential difference between two points along the flow direction of the system and is usually given by their pressure difference $\Delta P$ which is proportional to the flow rate ($Q$) and the fluidic channel geometry, and hence defines the local flow velocity ($u$) for a laminar system.

$$\Delta V_{str} = \frac{\varepsilon \sigma \Delta P}{\eta u}$$

Here, $\varepsilon$ is the relative permittivity of the electrolyte solution, $\varepsilon_0$ is the vacuum permittivity ($F/m$), $\zeta$ is the zeta potential of the EDL (V), $\sigma$ is the electrical conductivity of the bulk solution ($S/m$) and $\eta$ is the dynamic viscosity of the solution (Pa s). For SiO$_2$, which isoelectric point is around pH 2–3, the surface is negatively charged in an electrolyte of higher pH, resulting in a drag on the fluid moving along the flow direction. As $\zeta$ and $\sigma$ are directly affected by the ionic strength of the electrolyte solution, $V_{str}$ is larger at low ionic strength (Kim et al., 2009). Potentiometric sensors often detect analytes in low ionic strength buffers (De et al., 2013; Duan et al., 2012; Stern et al., 2007b). In such conditions fluctuations in the flow velocity can affect the local surface potential and thus introduce noise. Changes in conductance of a FET-based biosensors such as SiNWs, CNT, and InAs NWs have been reported when a stationary potential was generated by a fluidic flow in a microfluidic channel (Bourlon et al., 2007; Chen et al., 2013b; Kim et al., 2009; Newaz et al., 2012). This results in an undesirable change in surface potential of biosensors, interfering with the actual signal from the charged target molecules.

In this work we present a simple method to minimize streaming potential and thereby reduce its effects when measuring in electrolyte solutions with ultra-low ionic strength. Using a thin-film metal coating in the microfluidic channel, we effectively increase its conductivity. This results in a significant reduction of the local $V_{str}$ throughout the microchannel without affecting the sensor properties. Moreover, we demonstrate the reduction of noise introduced by incontinuous pumping by up to four orders of magnitude.

2. Material and methods

2.1. Measurement setup

We developed a multiplexed detection setup to concurrently measure up to 32 devices. Each amplification channel consists of a quad low noise operational amplifier (LT1125) configured as a current-to-voltage converter which feeds into a 32 channel multiplexer (MUX) (ADG732BSUZ) as depicted in Fig. 2a. The resistor ($R = 1$ MΩ) was chosen to match typical drain currents of ~100 nA such that the gain would be $10^6$ (0.1 μA of input current corresponds to 0.1 V output voltage). The capacitor was chosen for low pass filtering with a cutoff frequency at 1.59 Hz. In order to improve the portability and the noise performance of the measurement setup, the amplification stage was combined with the MUX in a custom designed printed circuit board (PCB) as shown in Fig. 2b. The SiNW biosensor chip was wire-bonded and inserted into a 68-pin leadless chip carrier (LCC) on the PCB. The board was connected to a portable USB National Instruments Data Acquisition (NI USB DAQ) Card via a 68-pin VHDCI connector from NI. A custom Labview software was written to interface and extract data from the 32 channel concurrently. The DAQ supplies the drain voltage ($V_D$, typically ~0.1 V) and the gate voltage ($V_G$, typically 0 to ~2 V) to the biosensor chip. The source current from each device is fed into the inverting terminal of the op-amp. Measurement data presented in this work was taken at a rate of 4 Hz/channel for real-time measurement. Deionized (DI) water (resistivity 17–18 $\Omega\text{cm}$) was used in this work was delivered to the chip through 24 gauge PTFE tubes. Solution delivery was achieved using a syringe pump (NE-1000, New Era Pump System, Inc.) or a piezoelectric micropump (mp6, Bartels). Ag/AgCl wires were inserted into the tubes as pseudo reference electrodes in order to control the electrical potential of the electrolyte solution.

2.2. SiNW fabrication

The p-type SiNW biosensors were fabricated on 8” silicon-on-insulator (SOI) wafers (SOITech) using a top-down method as reported in literature (Chua et al., 2009; Knopfmacher et al., 2010; Zhang et al., 2010). For scalability and to ensure compatibility with CMOS processing, we utilized a top-down deep UV optical lithography approach combined with interferometric masking and the self-limiting oxidation of silicon to form the NW arrays. The SOI wafer has typically 150 nm buried oxide with the active silicon layer ordinarily around 140 nm. We used atomic layer deposition of Al$_2$O$_3$ as the gate dielectric layer with typical thickness below 15 nm, and
SiO₂ was used as passivation layer to protect the metal contact leads. As shown in Fig. 2c, each SiNW device has 5 parallel wires for better device uniformity, stability and less performance variation in comparison with single NWs (Tian et al., 2011). The total length of the sensing area of a SiNW is 12 \( \mu \)m. Fig. 2d shows the transfer characteristics of the SiNW biosensor so nth es e m ch i pm e a s u r db yt h e multiplexed detection setup. Real-time measurement in this work was conducted in the linear region of the SiNW biosensors where the signal to noise ratio is maximized (Rajan et al., 2011).

2.3. Noise analysis

Fluctuations in the drain current were measured at 512 Hz/channel for 3000 s using the multiplexed measurement setup. The

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Fig. 2. Multiplexed detection setup and electrical characteristics of SiNW biosensors. (a) Schematic diagram of the multiplexed detection setup and (b) its photo image. (c) Microscope image of a SiNW biosensor consisting of five parallel wires. An opening in the protective SiO₂ layer is defined to expose the SiNWs to solution. (d) \( I_D-V_G \) (top) and transconductance (bottom) of 13 SiNW biosensors on the same chip.

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Fig. 3. SiNW surface potential changes due to changes in flow velocity in a microfluidic channel with two different widths. The SiNW position and reference electrode configuration strongly influence the effect of the streaming potential. (a) Fabrication process and the photo image for the Ag-coated PDMS microfluidic channel (100–1000 \( \mu \)m wide and 10 mm long channels). (b) Illustration of the three different measurement configurations used. Solution flows from left to right (small channel 100 \( \mu \)m, large channel 1 mm). The total length of the fluidic channel is 10 mm. The SiNW channel No. increases from inlet to outlet. (c–e) Case A: reference electrode at inlet. Case B: Ag-coated PDMS with potential applied to reference electrodes at inlet and outlet. Case C: Ag/Au/AgCl reference electrode.
data was translated into a current noise power spectral density ($S(f)$) via fast Fourier transform, using the Matlab analysis algorithm pwelch which implies smaller variance in the final power spectrum (Welch, 1967). The power spectral density of the gate referred noise ($S_{\text{f}}(f)$) was calculated by the formal relation: $S_{\text{f}}(f) = S(f)/g_m^2$, where $g_m$ is the transconductance (Ghibaudo, 1989).

3. Results and discussion

3.1. Streaming potential measurements

Fig. 3a shows the fabrication process flow and the photo image for the Ag-coated PDMS microfluidic channel (see Supplementary material). Fig. 3b illustrates 3 different measurement configurations regarding the position of the reference electrodes and the presence of the Ag layer in the PDMS fluidic channel. The SiNW devices are located in the center of the fluidic channel, and each measured device has 600 μm spacing. We conducted real-time current measurements of the SiNW biosensors as a function of flow velocity and extracted the surface potential ($\Psi_s$) of the sensor surface by dividing the drain current by $g_m$ for each device.

Fig. 3c shows the effect of changing streaming potential ($\Delta \Psi_{\text{str}}$) on $\Psi_s$ of the SiNW channels with changing flow rate when the reference electrode is placed at the inlet (Case A). Since the majority of the sensor chip is covered with a SiO$_2$ protection layer, which has an isoelectric point of ~2–3, the surface is negatively charged in DI water (pH ~ 5–6). The pressure-driven flow drags the excess counterions in the EDL downstream, building a positive $V_{\text{str}}$. The magnitude of the surface potential for each device increases as the flow rate gets higher since the streaming potential is proportional to the flow velocity. In the inset in Fig. 4b, the surface potential of the SiNWs in the small channel ($W = 100 \mu$m) increases linearly along the fluidic channel at fixed flow rate. The slope of $\Delta \Psi_s$ of the SiNWs in the wide channel ($W = 1000 \mu$m) is smaller than that of the small channel because the velocity becomes smaller due to 10 times wider width. Consequently, the observed surface potential change strongly suggests that the SiNWs are responding to the streaming potential change in respect to the flow rate, device location, and fluidic channel size. The ability to detect the local streaming potential enables the SiNWs to act as nanoscale flow sensors (Kim et al., 2009). In addition, the overall behavior of the streaming potential is observed when the reference electrode is located in the outlet as shown in Fig. S1 in the supporting information. In this case, the SiNWs are located upstream to the reference electrode. Hence, the surface potential is shifted negatively.

When two reference electrodes are applied at both inlet and outlet (Case B), the streaming potential can be reduced, as reported by Chen et al. (2013a). However, the SiNWs are affected by each electrode on either side, which means the electrostatic potential in the fluidic channel can adopt both upstream and downstream characteristics. As a result, the downstream potential change can be compensated by the upstream potential with respect to the outlet electrode. Fig. 3d shows that the surface potential of the SiNWs shows smaller fluctuations with changing flow rate while both electrodes are applied. The absolute value of the maximum $\Delta \Psi_s$ at a flow rate of 11 μl/min is almost 4 mV in the middle of the fluidic channel, approximately 40 times less than that of Case A. However, the effect of the streaming potential is still significant. A superposition of upstream and downstream potential could be expected along the microfluidic channel. The asymmetric channel structure and a small offset in electrochemical potential of the reference electrodes can explain the local differences in the streaming potential.

Fig. 3e shows the surface potential change of the SiNW in the Ag-coated microfluidic channel. The results clearly show that $\Delta \Psi_s$ is further suppressed as compared to Case B. The Ag layer between the reference electrodes increases the conductance and equalized the potential along the microfluidic channel. We emphasize that the Ag layer is not connected to the reference electrodes and its potential is solely defined by the solution in the microfluidic channel. The maximum fluctuation in surface potential is approximately 25% of Case B and almost 100 times smaller than Case A. The results imply that the Ag-coated microfluidic channel can eliminate the streaming potential regardless of the geometric structure of the microfluidics and small offsets in the electrochemical potential of the reference electrode.

3.2. Reduction of pump-induced noise

The use of micropumps is a promising approach for the realization of a portable biosensor. Piezoelectric micropumps enable fluid delivery at a wide range of flow rates, by applying an AC voltage to drive the expansion and compression strokes as the signal changes in polarity (Iverson and Garminella, 2008). However, even though piezoelectric micropumps have the advantage of miniaturization, low power consumption, and low cost, their operation principle generates large fluctuations in flow velocity. This
leads to additional noise associated with streaming potential fluctuations when measuring at low ionic strengths. To demonstrate the advantages of the Ag-coated microfluidic channel in alleviating these effects, we use a piezoelectric micropump to deliver DI water to the SiNWs and compare the performance of the noise reduction.

Fig. 4 shows the power spectral density of the gate referred noise $S_v(f)$ of the different SiNW channels while DI water was pumped through the microfluidic channel by applying a 1 Hz trapezoidal signal to the piezoelectric micropump controller (mp6-OEM, Bartels). The inset in Fig. 4a shows clear oscillations of the surface potential at 1 Hz induced by the pump. Accordingly, the power spectral density of the gate referred noise has its highest peak at the fundamental frequency (1 Hz) and contains both even and odd harmonics (Fig. 4a). The peak heights increase as the changes in streaming potential become more pronounced with increasing distance between the SiNW channel and the reference electrode. The maximum peak of $S_v(f)$ is $1.45 \times 10^{-2} (V^2/Hz)$ in the SiNW channel No.15 which is located furthest from the reference electrode as shown in Fig. 3b.

Fig. 4b shows that the use of an Ag-coated microfluidic channel significantly reduces the pump-induced noise. The inset indicates the surface potential fluctuation of the Ag-coated microfluidic channel to be approximately $10^2$ times smaller than that of the microfluidic channel without the Ag layer, as the effect of the streaming potential on the surface potential of the individual SiNW channels is eliminated. The averaged maximum peak of $S_v(f)$ at $f=1$ Hz is $1.35 \times 10^{-6} (V^2/Hz)$ which is $10^4$ times smaller as compared to Fig. 4a. It is important to note that the demonstrated thin metal layer in the microfluidic channel can simply achieve a dramatic reduction of the gate noise induced by fluctuations in streaming potential, caused by the piezoelectric micropump, without additional signal processing and/or off-chip circuitry.

4. Conclusions

In conclusion, we have demonstrated a simple yet effective method to minimize streaming potential in microfluidic channels and thereby reduce noise and superimposed signals of SiNW sensors when measuring in electrolyte solutions with ultra-low ionic strength. By depositing a thin Ag film on the microchannel surface, the fluidic channel's conductivity is increased and thereby the electrical potential along the fluidic channel is equalized, resulting in an effective reduction of the local streaming potential throughout the microfluidic channel without affecting the sensor properties. No surface treatment of the metal layer, such as chlorination, is needed as its potential is defined by the Ag/AgCl reference electrode via the solution. Furthermore, we demonstrated the reduction of the noise introduced by a piezoelectric micropump by up to four orders of magnitude. It should be noted that the reduction of the streaming potential is very important for potentiometric biosensors, as the streaming potential can easily exceed signals from a specific analyte-receptor binding event. The simple approach presented in this work is an effective method for eliminating the streaming potential and may find uses as a powerful tool in nanoscale potentiometric biosensor applications.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.bios.2016.08.065.

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