

## Systematic Optimization for the Design of Si-NW Biosensor

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### ABSTRACT

**Biomolecular analysis at very low concentrations is becoming increasingly important. Semiconducting nanowires have been reported as highly sensitive biosensors. Biosensor based on Si-NW has already demonstrated ultrasensitive detection of DNA, proteins, pH levels, etc. Although it is generally accepted that NWs with lower doping density and smaller diameter provides better sensitivity, the influence of factors like electrostatic screening due to the ions in the solution, analyte concentration, pH of the electrolyte solution on NW sensor performance needs to be explained for the systematic optimization of sensor design. In this theoretical study a simple analytical model, based on reaction-diffusion theory is developed to obtain the minimum detectable concentration by a Si-NW biosensor. Investigating the average response time this study shows that, for a reasonable incubation time (500 sec), Si-NW sensor can detect down to about 350 fM concentrations. Also the Poisson Boltzmann Equation is solved analytically based on the result of the diffusion-capture model to show that the electrostatic screening within an ionic environment limits the response of a Si-NW biosensor. In this research work, maximum pH sensitivity achieved for Si-NW sensor is 45 mV/pH. This study concludes that, the parameters such as the dimension of the Si-NW, the doping level of the Si-NW, analyte concentration, the ions concentration in the solvent, pH of the solution etc must be optimized for high sensitivity biomolecule detection.**

**Keywords:** Si-NW, Sensitivity, P Electrostatic screening, Poisson Boltzmann Equation.

### 1. Introduction

Electronic detection of biomolecules in the solvent is one of the widely studied topics in recent years. Systems based on nanoscale devices can provide fast, low-cost, and high throughput analysis of biological processes and are gaining importance due to their large potential in commercial applications [1]. Since the early 1970s, the basic idea of ion-sensitive field-effect transistor (ISFET) has been realized based on metal oxide silicon field-effect transistor (MOSFET) [2]. In an ISFET the gate structure of a MOSFET is replaced by a biomaterial layer (ion-selective layer), electrolyte and a reference electrode. The ISFET can measure the concentration of certain ion species in the electrolyte, such as protein, enzyme and DNA [3]. However, several disadvantages, such as lack of good solid state electrodes, parasitic sensitivity to temperature and light, time dependent instability of sensor parameters, have restrained the development of ISFET as a popular biosensor technology [4].

Silicon nanowire field-effect transistor (SiNW FET) biosensors have recently been demonstrated experimentally for direct, label free, high sensitive, high selective and real time detection of DNA and proteins at very low concentration [5]. Because of the small size and large surface-to-volume ratio of the Si-NW, the detecting sensitivity is increased as compared with traditional ISFET biosensors [1]. The major advantage of Si-NW biosensors is the label free operation, the high sensitivity and the real time and continuous operation. As DNAs are highly charged biomolecule the detection of DNA is of special interest and is widely demonstrated as a model system to

study biorecognition with other biomolecules [1]. For target DNA detection using ss DNA as receptors, the ion concentration of the solution has to be quite high to ensure the conjugation between the negatively charged target and receptor strands [6]. Many parameters affect the performance of Si-NW biosensor, such as the dimension of the Si-NW, the doping density of the Si-NW, the surrounding environment (the ions concentration in the solvent) [5]. These parameters need to be investigated for the systematic optimization of biosensor design.

In this theoretical study, a comprehensive modeling theory and simulation approach is proposed to account for the underlying electrical detection mechanism of DNA using Si-NW biosensor. The theory is based on self-consistent solution of the diffusion-capture model and Poisson Boltzmann Equation. The D-C Equations are solved analytically to determine the minimum detectable concentration by Si-NW biosensor. The Poisson Boltzmann Equation is derived from the classical Poisson Equation using the Boltzmann distribution to model the charge distribution in the ionic solvent. The analytical solution to the Poisson Boltzmann Equation is discussed to illustrate the importance of screening-limited kinetic response of Si-NW sensor. The simulation results are analyzed and the influence of parameters like the dimension of the Si-NW, the doping of the Si-NW, and surrounding environment (the ions concentration in the solvent) are investigated for the performance optimization of the Si-NW biosensor.

### 2. Si-NW System

Figure 1 shows a schematic of a Si-NW biosensor. The system consists of a Si-NW core between two electrodes, a

surrounding silicon oxide layer, a layer of biomaterial, and surface receptor biomolecules. The configuration and the underlying detection mechanism of Si-NW biosensor are similar to that of a Si-NW FET [7]. A Si-NW FET, whose conductance is modulated by an applied gate voltage, is transformed into a biosensor by modifying the silicon oxide surface with a layer of biomaterial, and surface receptor biomolecules. The binding of a charged biomolecules (target biomolecules) to the gate dielectric is analogous to applying a voltage using a gate electrode.

A general scheme for detecting biomolecules using Si-NW sensor is shown in Figure 2. The surface of the nanowire is functionalized with specific receptors that recognize and bind only to the target molecules. The electrodes are protected from the solution by an oxide layer to avoid any undesired conductance change due to modification of electrode work function [8]. When the sensor is immersed in an analyte solution some of the target molecules diffuse through the solution and reach the NW and get captured by the receptors and thereby binding them close to the surface. Many biomolecules carry an electrostatic charge under normal physiological conditions. The Coulomb interaction between the charge of the target biomolecule and the NW can result in a change in conductivity of the latter.

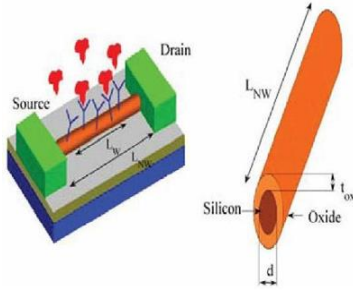


Fig. 1: Schematic of a Si-NW biosensor

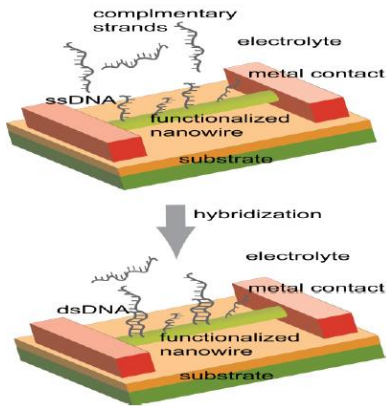


Fig. 2: Operation of Si-NW biosensors.

### 3. System Modeling

#### 3.1 Diffusion-Capture Model

Time dynamics of molecule capture on a sensor surface is two step processes [9]: transport of the target molecules to the sensor surface and the subsequent conjugation with the receptor molecules. Consider an isolated sensor immersed in a static analyte solution at time  $t=0$  (Figure 1). The

Diffusion-Capture (D-C) model assumes that the molecule transport is diffusion limited and the target-receptor conjugation is treated as a first-order chemical reaction [10]. The rate of conjugation between the target and the receptors is given by Equation (1).

$$\frac{dN}{dt} = k_F(N_0 - N)\rho_s - k_R N \quad (1)$$

where  $N$  is the density of conjugated receptors,  $N_0$  is the density of receptors on the sensor surface,  $k_F$  and  $k_R$  are the capture and dissociation constants (forward and reverse reaction coefficients), and  $\rho_s$  is the concentration of analyte particles at the sensor surface at any given time  $t$ .  $\rho_s$  is determined by the diffusion of target molecules set by the concentration gradient at the sensor surface which is given by Equation (2).

$$\frac{d\rho}{dt} = D\nabla^2\rho \quad (2)$$

where  $D$  is the diffusion coefficient of target molecules in the solution that depends on the fluidic environment and size of the target biomolecule. Analytical solution of Equation (1) and (2) gives the transient response of Si-NW sensor given by Equation (3).

$$N(t) = \rho_0 t \left( \frac{a_0 \log\left(\frac{\sqrt{4Dt} + a_0}{a_0}\right)}{D} + \frac{1}{k_F N_0} \right)^{-1} \quad (3)$$

where  $a_0$  is the radius of the nanowire. Define the number of analyte particles required to capture for minimum amount of detectable signal change as  $N_s$ . Then the time required to capture  $N_s$  particle is defined as settling time ( $t_s$ ). Then approximating  $1/k_F N_0 \approx 0$ , the settling time for cylindrical Si-NW sensor can be calculated from Equation (4).

$$t_s \cong \frac{N_s a_0 \log[(\sqrt{4Dt_s} + a_0)/a_0]}{\rho_0 D} \quad (4)$$

#### 3.2 Model Based on Poisson-Boltzmann Equations

Consider a Si-NW sensor is immersed in an electrolyte solution whose surface is functionalized with specific receptor. Figure 3(a) shows the Cross-section of the sensor and Figure 3(b) shows the charge distribution inside the three sub-regions of the system (1) cylindrical Si-NW of diameter  $d$ ; (2) insulating native oxide around the NW of thickness  $t_{OX}$ ; and (3) electrolyte that contains the target biomolecules, and the various ions that provide the necessary buffer for the stability of target-receptor binding.

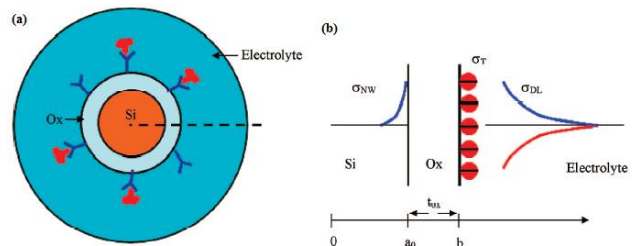


Fig. 3: Schematic of Si-NW biosensor. (a) Cross-section of the sensor (b) Charge distribution in the sensor system.

The non-linear Poisson-Boltzmann Equation governing the electrostatic potential in all the three regions is given by Equation (5) [11].

$$-\nabla \cdot (\varepsilon(r) \nabla \varphi(r)) + 2 \alpha(r) q I_0 N_{avo} \sinh\left(\frac{q\varphi(r)}{k_B T}\right) = q \sum_i^N Z_i \delta(r - r_i) \quad (5)$$

Where the parameter  $\alpha(r)$  and piecewise dielectric constant function  $\varepsilon(r)$  are given by:

$$\varepsilon(r) = \begin{cases} \varepsilon_{Si} & \text{for region 1} \\ \varepsilon_{OX} & \text{for region 2} \\ \varepsilon_w & \text{for region 3} \end{cases}$$

and

$$\alpha(r) = \begin{cases} 0, & \text{for region 1 and 2} \\ 1, & \text{for region 3} \end{cases}$$

Where,  $k_B$  is the Boltzmann constant,  $T$  is the temperature, and  $q$  is the electronic charge ( $1.6 \times 10^{-19}$  C),  $I_0$  is the ion concentration in molar units, and  $N_{avo}$  is the Avogadro's constant, whereas the sinh term denotes the contribution due to a 1-1 electrolyte (e.g., Na<sup>+</sup> - Cl<sup>-</sup>), whose ions are assumed to follow Boltzmann distribution [1]. The right-hand side denotes the fixed charge due to the biomolecule,  $Z_i$  and  $r_i$  denoting the partial charge and location of the atoms within the biomolecule, respectively.

If ion concentration in the electrolyte is zero ( $I_0 = 0$ ), the charge density ( $\sigma_T$ ) due to analyte molecules on the sensor surface is equal to the charge induced in the sensor ( $\sigma_T = -\sigma_{NW}$ ). The charge density due to analyte biomolecules is given by Equation (6).

$$\sigma_T \cong \sigma_S N(t) \quad (6)$$

where,  $\sigma_S$  is the charge of a biomolecule. It is important to note that  $\sigma_T$  has been approximated by the charge due to captured biomolecules only. The induced charge density of a heavily doped cylindrical NW can be calculated by using the formula for capacitance of oxide dielectric on cylindrical NW as Equation (7) [12].

$$\sigma_{NW} = -\frac{\varepsilon_{OX}}{(a_0 + t_{OX}) \log(1 + \frac{t_{OX}}{a_0})} \varphi_0 \quad (7)$$

Where  $\varphi_0$  is the surface potential,  $a_0$  is the nanowire radius and  $t_{OX}$  is the thickness of the oxide layer. From Equation (6) and (7) the electrostatic potential is found from Equation (8):

$$\varphi_0 = \frac{\sigma_S N(t) (a_0 + t_{OX}) \log(1 + \frac{t_{OX}}{a_0})}{\varepsilon_{OX}} \quad (8)$$

The sensitivity  $S$  of a Si-NW sensor is defined as the relative change in conductance  $S = \nabla_G / G_0$  Where the conductance of a cylindrical Si-NW of radius  $a_0$ , uniform continuous doping density  $N_D$ , and length  $L_{NW}$  is given by  $G_0 = q\mu N_D \pi a_0^2 / L_{NW}$  and the change in conductance is determined by assuming that the molecule conjugation on the surface is approximated by a constant surface density  $\sigma_{NW}$  (in charge per square centimeter) as  $\nabla G =$

$2\pi a_0 \mu \sigma_{NW} / L_{NW}$ . where  $\mu$  is the mobility of the carriers. Then using Equation (7) and (8) the sensitivity of the Si-NW sensor is obtained as Equation (9).

$$S = \frac{2\sigma_S N(t) (a_0 + t_{OX})}{q a_0^2 N_D} \quad (9)$$

The full charge of the captured biomolecules is not effective in modulating the conductance of sensors due to the electrostatic screening of ions present in the electrolyte. To account for screening, one must solve the nonlinear Poisson-Boltzmann Equation for region 3 (Equation 10) [12].

$$-\nabla^2 \varphi(r) + \frac{k^2}{\beta} \sinh(\beta \varphi(r)) = \frac{q}{\varepsilon_w} \sum_i^N Z_i \delta(r - r_i) \quad (10)$$

where,  $k^2 = 2q^2 I_0 N_{avo} / \varepsilon_w k_B T$  and  $\beta = q / k_B T$ . Applying the Charge conservation rule to the system ( $\sigma_T = -(\sigma_{DL} + \sigma_{NW})$ ), Screening limited kinetic response of nanobiosensors may be obtained as in Equation (11).

$$\frac{\varepsilon_{OX}}{(a_0 + t_{OX}) \log(1 + \frac{t_{OX}}{a_0})} \varphi_0 + \frac{2\varepsilon_w k}{\beta} \sinh\left(\frac{\beta \varphi_0}{2}\right) \sqrt{1 + \frac{\gamma^{-2} - 1}{\cosh^2(\frac{\beta \varphi_0}{2})}} = \sigma_S N(t) \quad (11)$$

where  $\sigma_{DL}$  is the net charge in the electrical double layer formed at the sensor surface (which represents the screening due to the ions in the electrolyte). At equilibrium the concentration of conjugated biomolecule is found from D-C model as  $N_{equi} = k_F N_0 \rho_0 / (k_F \rho_0 + k_R)$ . The steady-state response can be obtained by replacing  $N(t)$  in the right-hand side of Equation (11) with  $N_{equi}$ . Solving Equation (11) and substituting the solution for  $N(t)$  into Equation (9), the screening-limited sensitivity for Si-NW sensor is obtained as function of analyte concentration and ion concentration and is given by Equation (12)

$$S = C_1 \left[ \ln(\rho_0) - \frac{\ln(I_0)}{2} + C_2 \right] \quad (12)$$

$$\text{where } C_1 = \frac{4\varepsilon_{OX}}{\beta q a_0^2 N_D \log(1 + \frac{t_{OX}}{a_0})}$$

and

$C_2 = \ln\left[\frac{\sigma_S k_F N_0}{k_R} \sqrt{\frac{\beta}{2\varepsilon_w q N_{avo}}}\right]$ . The net charge density (charge density due to analyte molecules) on the NW surface can be obtained based on first-order chemical kinetics of bond dissociation for the particular type of surface functionalization schemes used (-OH, -NH<sub>2</sub>, etc.). The net charge density ( $\sigma_{pH}$ ) on the sensor surface is given by Equation (13) [13]:

$$\sigma_{pH} = q N_F \exp(\varphi_0 + 2.303(pH - pKa)) \quad (13)$$

where  $pKa = -\log_{10} K_a$ ;  $K_a$  is the dissociation constant and  $N_F$  is the density of surface functionalization groups. Then by replacing  $\sigma_S N(t)$  from the right-hand side of Equation (11) with  $\sigma_{pH}$  the screening-limited sensitivity for Si-NW sensor is obtained as function of pH and ion concentration and is given by Equation (14)

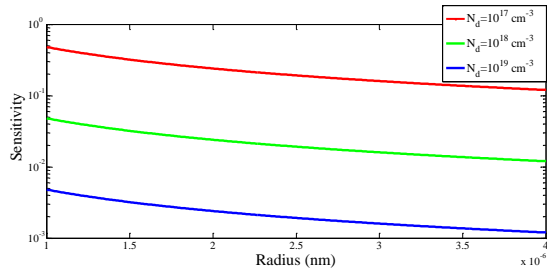
$$S = C_1 \left[ C_3 + \frac{\ln(I_0)}{2} - 2.303(pH - pKa) \right] \quad (14)$$

where the constant  $C_3$  is given as:  $C_3 = \frac{1}{2} \ln(2\epsilon_w N_{avo} / q\beta N_F^2)$

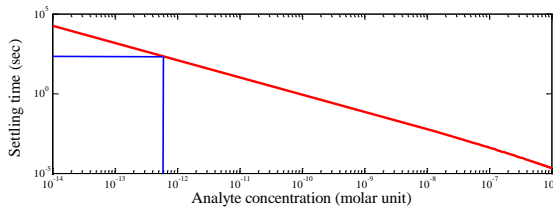
#### 4. Result Analysis

The design of a nanoscale biosensor greatly depends on the dimension of the nanostructures, their doping density and also the parameters (analyte concentration, ion concentration, pH of the solution, etc.) related to the sensor application environment that seriously affect the sensor performance. Although analytical solution of the model based on diffusion capture Equations and Poisson-Boltzmann Equation provide a rough theoretical estimate for the performance parameters of nanobiosensors, the implications of this model are actually profound and it gives one a very sophisticated understanding of electronic biosensing.

The most attractive feature of nanoscale biosensor is that its performance improves as the diameter of the nanowire as well as doping density decreases. Figure 4 shows the sensitivity of Si-NW sensor increases as radius of the NW decreases for three different doping levels ( $N_d = 10^{17} \text{ cm}^{-3}$ ,  $10^{18} \text{ cm}^{-3}$  and  $10^{19} \text{ cm}^{-3}$ ). Nanowire length is kept constant ( $2 \mu\text{m}$ ) and air is assumed as the surrounding medium of the nanowire. Figure 4 clearly shows that sensitivity increases with smaller diameter and reduced doping density, which is consistent with Equation (9) and almost similar results also observed in a recent work [1].



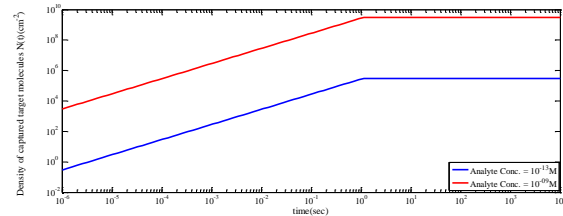
**Fig. 4:** Sensitivity of NW sensor as function of radius.



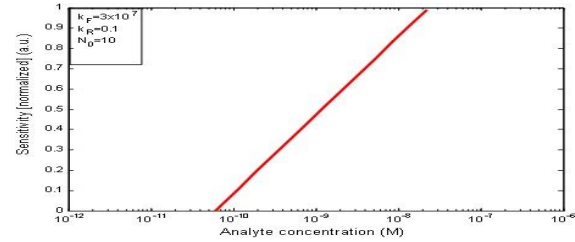
**Fig. 5:** Response time for Si-NW sensor as function of analyte concentration.

Figure 5 allows one to predict the minimum detectable concentration for cylindrical Si-NW sensors for a typical DNA detection problem. It is found that, for a reasonable incubation time (500 sec), cylindrical Si-NW sensor can detect down to about 350 fM concentrations. Thus there exist fundamental limits in the concentration of biomolecules which can be detected by any sensor under reasonable settling time. The detection limit of a typical 2D nanowire sensor (for the same response time) is three to

four orders of magnitude higher compared to planar 1D sensor [7].



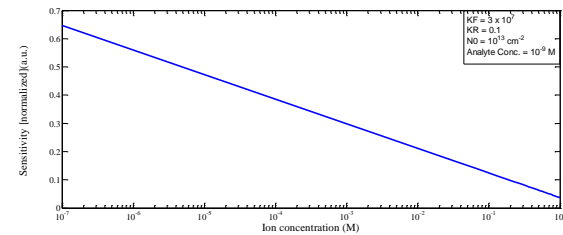
**Fig. 6:** Transient response for cylindrical Si-NW sensor.



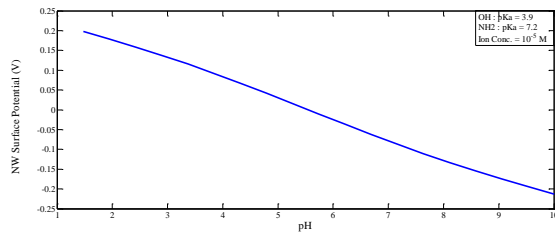
**Fig. 7:** Sensitivity versus analyte concentration for constant ion concentration ( $10^{-3} \text{ M}$ )

Figure 6 shows the transient response Si-NW biosensor for two different analyte concentrations (100 fM and 1 nM). It is seen that, sensor response improves as time goes and become saturated after a certain time. This saturation is due to the balance of forward and backward reaction. It is observed that the number of captured analyte molecules increases with analyte concentration as expected. Figure 7 shows that sensitivity improves as target molecule density increases. The ratio of the reaction coefficients ( $k_F/k_R$ ) is taken as  $3 \times 10^8$ . Water is considered as the surrounding medium. Dielectric constant of water is  $\epsilon_w = 80\epsilon_0$  and dielectric constant of the oxide layer ( $\text{SiO}_2$ ) is  $\epsilon_{OX} = 3.9\epsilon_0$ . For all cases the receptor density on the sensor surface is taken  $10^{12} \text{ cm}^{-2}$ . The ion concentration is taken  $10^{-3} \text{ M}$ . The graph shown in Figure 7 clearly shows that due to the electrostatic screening of ions in the solvent minimum detectable concentration cannot be achieved at the desired level.

Figure 8 shows the dependence of sensitivity on ion concentration. The result is obtained by solving the analytical Equation (12) at analyte concentration  $10^{-9} \text{ M}$  and  $k_F/k_R$  ratio  $3 \times 10^8$ . It is obvious that sensitivity decreases with increasing ion concentration. This is reasonable because screening by the ions reduces the overall charge effective in modulating sensor response.



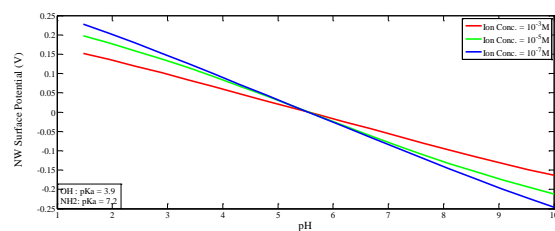
**Fig. 8:** Sensitivity changes with ion concentration



**Fig. 9:** NW surface potential versus pH of electrolyte solution

Figure 9 shows nanowire surface potential changes linearly with pH of the solution. This study is based on the first order chemical kinetics of bond dissociation for the functionalization groups of  $-\text{OH}$  and  $-\text{NH}_2$ . For  $-\text{OH}$  and  $-\text{NH}_2$  groups, pKa values are taken 3.9 and 7.2 respectively. Ion concentration is kept constant ( $10^{-5}\text{M}$ ). The density of surface functionalization groups is considered  $10^{14}\text{cm}^{-2}$ . It is demonstrated that, surface potential decreases as pH of the solution increases. This is obvious because high pH of the solution means the high concentration of  $-\text{OH}$  ion in the solution and high ion concentration lower the surface potential by decreasing the charge effective in conductance modulation. The slope of the line gives the rate of change of surface potential with pH ( $\sim 45\text{ mV/pH}$ ). The pH sensitivity obtained by some research group is very close to this value [14].

Figure 10 shows the change in surface potential with pH of the electrolyte solution at three different ion concentrations ( $10^{-3}\text{M}$ ,  $10^{-5}\text{M}$  and  $10^{-7}\text{M}$ ). It is seen that at higher pH value surface potential increases with ion concentration but at lower pH value it slightly reduces with ion concentration. From the figure it is investigated that at pH value of 5.5 surface potential is zero but when the pH value decreases or increases from that value surface potential changes quickly with pH. Therefore for better sensitivity, biomolecule detection should be done at pH away from pH value 5.5.



**Fig. 10:** NW surface potential versus pH of electrolyte solution for three different ion concentrations.

## 5. Conclusion

Investigating the performance parameters of Si-NW biosensor is very enthusiastic since the device has many aspects that can be explored and improved. The model developed in this research investigates the detection limits of Si-NW biosensor. For reasonable incubation time the Si-NW sensor can detect down to femto-molar concentration. The maximum pH sensitivity by Si-NW sensor is achieved in this research is  $45\text{ mV/pH}$ . The sensitivity of Si-NW biosensor increases with reduced doping and smaller diameter. The response of Si-NW sensor greatly depends on

the buffer ion concentration and pH of the electrolyte solution. As a conclusion, to design highly sensitive biosensor using Si-NW one must systematically optimize sensor response as a function of sensor geometry, fluidic conditions, and the ion concentration in the aqueous solution.

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