Principles of Electronic Nanobiosensors

Unit 3: Sensitivity
Lecture 3.6: Potentiometric Sensors: How to Beat Screening

By Muhammad A. Alam
Professor of Electrical and Computer Engineering
Purdue University
alam@purdue.edu
Outline

• Challenges of charge screening

• Techniques to overcome screening
  – De-screening of DNA at high frequencies
  – Device Approach: Giant Nernst Sensor
  – Tag-based approach

• Conclusions
DNA binding and Salt screening
De-screening at High Frequencies

At 1 MHz, molecules are frozen, but the dipoles are not

\[ \phi = \phi_0 \frac{1}{1 + r/L_D} \]

100 mM gives \( \sim 1 \) nm.

\[ L_D = \sqrt{\frac{k_W \varepsilon_0 k_B T}{q^2 I_0}} \]

\[ \phi = \phi_0 e^{-x/L_D} \]

Screening is frequency dependent

Potential Distance

Capacity (F) vs Frequency (Hz)

Small signal

Distance Potential

$\sim L_D$

Distance Potential

Distance Potential
Screening is frequency dependent

\[ C_{DL} = \sqrt{\frac{2q^2\epsilon_wN_{av}I_0}{kT}} \cosh \left( \frac{qV}{kT} \right) \]

\[ G \propto 2qN_{av}I_0\mu \]
Why is the critical frequency?

\[ C_{DL} = \sqrt{\frac{2q^2 \varepsilon_w N_{av} I_0}{kT}} \cosh\left(\frac{qV}{kT}\right) \]

**Graph:**
- **Capacitance (F) vs. Frequency (Hz)**
- **G/C_{DL}**

**Legend:**
- **G \propto 2qN_{av}I_0\mu**
- **Salt concentration**
- **Mass of the salt molecule**
Strategy of high frequency descreening

(1) \( V_D = \nu_{ac} \left[ 1 + m \cos(\omega_m t) \right] \cos(\omega_c t) \)

(2) Sets up an oscillation

(3) Dipole modulates the channel potential

(4) \( I_{s_m} = \gamma \frac{m \mu C_g}{2L} \nu_{ac} \phi(p) \cos \theta \)
Outline

• Challenges of charge screening

• Techniques to overcome screening
  – De-screening of DNA at high frequencies
  – Device Approach: Giant Nernst Sensor
  – Tag-based approach

• Conclusions
Recall: Nernst Limit of an ISFET

\[ I_D \propto Q_s = Q_s^+ - Q_s^- = f \left\{ [H^+]_S \right\} \]

\[ [H^+]_S = [H^+]_B e^{-q(\psi_0 - V_{FG})/k_BT} \]

\[ [H^+]_B \equiv e^{-2.303pH} \]

\[ I_{D1} \propto Q_{s1} \sim f(x_1) \quad x_1 = e^{-2.303pH_1 - q(\psi_{01} - V_{FG1})/k_BT} \]

\[ I_{D2} \propto Q_{s2} \sim f(x_2) \quad x_2 = e^{-2.303pH_2 - q(\psi_{02} - V_{FG2})/k_BT} \]

\[ I_{D1} = I_{D2} \Rightarrow \psi_{0,1} = \psi_{0,2} \]

\[ \Delta V_G \approx 2.303(k_B T / q) \Delta pH \]

\[ \Delta V_G / \Delta pH = 59 mV / pH \]

Alam, Principles of Nanobiosensors, 2013
Amplification with Double-gate FET

$$\Delta V_{G,1}$$

$$\Delta I_{D,top} = \mu_1 C_{tox} \left(\frac{W}{L}\right)_1 V_{DS,1} \Delta V_{G,1}$$

$$\Delta I_{D,bot} = \mu_1 C_{box} \left(\frac{W}{L}\right)_1 V_{DS,1} \Delta V_{G,2}$$

$$\Delta I_D = \Delta I_{D,top} + \Delta I_{D,bot} = 0$$

$$\Delta V_{G,1} / \Delta p\text{H} = 59 \text{mV} / \text{pH}$$

$$\frac{\Delta V_{G,2}}{\Delta p\text{H}} = 59 \frac{\text{mV}}{\text{pH}} \times \left(\frac{C_{tox}}{C_{box}}\right)$$
Experimental demonstration for DGFET

$$\frac{\Delta V_{G,2}}{\Delta pH} = 59 \frac{mV}{pH} \left( \frac{C_{tox}}{C_{box}} \right) = 59 \frac{mV}{pH} \left( \frac{T_{box}}{T_{tox}} \right)$$

Equivalent to changing the top gate bias
Amplification by a NP-NW Sensors

Accumulation mode operation

\[ \Delta I_{D,1} = \mu_1 C_{OX,1} \left( \frac{W}{L} \right)_1 V_{DS,1} \Delta V_{G,1} \]

\[ \Delta I_{D,2} = \mu_2 C_{OX,2} \left( \frac{W}{L} \right)_2 V_{DS,2} \Delta V_{G,2} \]

\[ \frac{\Delta V_{G,2}}{\Delta V_{G,1}} = \left( \frac{\mu_1}{\mu_2} \left( \frac{W}{L} \right)_1 \frac{V_{DS,1}}{V_{DS,2}} \right) \frac{C_{OX,1}}{C_{OX,2}} \]

\[ \frac{\Delta V_{G,2}}{\Delta pH} = \frac{\Delta V_{G,1}}{\Delta pH} \times \alpha_{GN} \times \frac{C_{OX,1}}{C_{OX,2}} \]

\[ \frac{\Delta V_{G}^{NP-NW}}{\Delta pH} = 59 \frac{mV}{dec} \left( \frac{C_{OX,1}}{C_{OX,2}} \right) \alpha_{GN} \]

\[ \Delta I_D = \Delta I_{D,1} + \Delta I_{D,2} = 0 \]
Signal to Noise Ratio in a pH amplifier
Signal to Noise Ratio in a pH-Amplifier

(a) Measured sensitivity (NP)
(b) Measured sensitivity (NP-NW)

Instrument noise
Intrinsic noise (NP-NW)

Alam, Principles of Nanobiosensors, 2013
Conclusions

• Screening of biomolecules is reduced at high frequencies because the screening charges cannot respond fast enough, exposing the entire charge sequence temporarily. Sensors with

• Giant Nernst Response amplifies signal electronically to improve sensitivity to pH changes. However, SNR is improved only for special cases.

• Amperometric and cantilever sensors do not suffer from screening limits (but diffusion limit still applies). We will discuss them next.