Controlling surface-enhanced charge screening to realize single-molecule sensing with silicon FET sensors

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1. Introduction

Large-scale single-molecule sensing to enable & boost applications in the life sciences (e.g. SMRT sequencing)

Silicon Field-Effect Transistor (FET) sensor:
- Real-time charge-based sensing of biomolecules and/or ions
- Paragon of embeddable & scalable technology
- Unprecedented throughput & parallelism

No single-molecule detection achieved

Main sensitivity-limiting factor is electrolyte charge screening
- Enhanced by charged and pH-sensitive oxide surface sites
- Non-linear screening and pH feedback effect

2. FET sensor modeling

a. Non-linear screening
- Formation of electrical double layer at charged entity
- Screening by near-exponential distribution of ions
- Increased ion concentration ($c_\pm$) in diffuse layer enhances electrolyte screening

Bikerman model:

\[
\begin{align*}
c_\pm &= c_0 \exp \left( \frac{\pm q \psi}{kT} \right) \\
c_0 &= \text{bulk ion conc.}
\end{align*}
\]

b. pH feedback effect
- Biomolecule charge alters local proton conc. ($[\text{H}^+]_{\text{int}}$) or pH at the FET surface
- pH-sensitive oxide surface sites induce a counter charge

For SiO$_2$:

\[
K_a = \frac{[\text{H}^+]_{\text{int}}[\text{SiOH}^-]}{[\text{H}^+]_{\text{int}}[\text{SiOH}^-] + [\text{H}^+]_{\text{int}}[\text{H}^+]_{\text{int}}}
\]

\[
pK_a = 4.5
\]

3. Single-molecule TCAD simulation

a. finFET with discrete biomolecule
- 15bp dsDNA = 30 charges
- 1.5 mM salinity and pH 7

b. Simulation of single-molecule SNR
- Signal is $\Delta V_g$ of $I_d-V_g$ curve due to charge of biomolecule
- Noise is $\Delta V_{\text{trap}} = \sqrt{D_{\text{trap}}A_{\text{eff}}}$

4. Results and discussion

pH-insensitive surface sites
- 8x boost in signal and SNR

Uncharged surface sites
- Extra 2x boost in signal and SNR

Noise unaffected

To boost FET single-molecule sensitivity, one must select a gate oxide with lowly-charged and pH-insensitive surface sites