Electrolyte-Gated FET-based Sensing of Immobilized Amphoteric Molecules Including the Variability in Affinity of the Reactive Sites

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***Abstract*— In this work, we developed a unique computational approach that allowed us to detect immobilized amphoteric molecules on the surface of an electrolyte-gated FET-based sensor. Our simulation methodology is based on a combination of the Site-Binding and Gouy-Chapman-Stern models which are solved self-consistently. Our analytical model allows us to describe the surface charge density due to the protonation and deprotonation of the reactive sites of amphoteric molecules. Moreover, we have analyzed the effect of variability in the affinity constant of reactive sites. We also studied the effect of random dopant fluctuations in nanowire FET to account for the reliability issues in FET-based sensor technology.**

I. Introduction

Amphoteric molecules are found in a variety of biological and chemical systems, including amino acids, proteins, and surfactants. Amphoteric molecules also have potential applications in the development of sensors and biosensors [1]. For example, amphoteric molecules can be immobilized on a sensing surface and used to detect specific proteins or nucleic acids in biological samples. However, the affinity of amphoteric molecules can vary greatly, leading to different sensitivities and selectivities of detection. One important factor that affects the variability in the affinity of amphoteric molecules' reactive sites is the local environment of the molecules, such as pH, temperature, and solvent composition [2]. By gaining a deeper understanding of the factors that affect the affinity of reactive sites, we can develop improved sensing platforms that have a wide range of applications sensing.

II. Methodology

We report a unique methodology based on the Site-Binding and Gouy-Chapman-Stern models which are solved self-consistently to generate our analytical model for the signatures of amphoteric molecules [3][4]. As an example, for amphoteric molecules, we analyzed three amino acids for which the calculated surface charge density (σ_o) is different for considered amino acids [Asparagine (σ_{o1}), Cysteine (σ_{o2}) and Lysine (σ_{o3})] excluding the effect of the immobilized carboxylic terminal [5].

$$\sigma_{o1} = qN_S\left(\frac{cH_S}{cH_S + K_a}\right) \quad (1) \qquad \sigma_{o2} = qN_S\left(\frac{cH_S^2 - K_aK_b}{cH_S^2 + cH_S K_a + K_aK_b}\right) \quad (2)$$

$$\sigma_{o3} = qN_S\left(\frac{cH_S^2 + cH_S K_a}{cH_S^2 + cH_S K_a + K_aK_b}\right) \quad (3)$$

III. Results and Discussion

As shown in Fig. 1 (a)(b) and (c), the solid line represents the surface potential (Ψ_o) which clarifies the presence of different reactive sites on the considered carboxylic-terminal (C-Imm.) immobilized amino acids [5]. The presence of α-amine reactive sites in C-Imm. N shows the Ψ_o variation from positive to zero value due to protonation and deprotonation with respect to bulk pH respectively. Due to an extra amine reactive site as a sidechain, the deprotonation requires a higher pH for C-Imm. K as compared to C-Imm. N. The presence of sulfur sidechain in C-Imm. C and its deprotonations allow the σ_o to take negative values. 2nd order gradient of surface potential ($d^2\Psi_o/dpH^2$) shows the exact correlation of affinity constants of the amino acids with the zero-crossover points. Similarly, C_T consists of differential capacitance along with the intrinsic capacitance due to the length and permittivity of the amphoteric molecule, for which the minimum of the normalized C_T signifies approx. isoelectric point. Fig. 2 and Fig. 3 show the $d^2\Psi_o/dpH^2$ for amino acids with amine sidechain (eg. Lysine) and carboxylic sidechain (eg. Cysteine) respectively. For the affinity constant variations, the pK_a is kept the same to values 3, 7, & 11 and pK_b is varied throughout the pH range which shows that as the pK values get close to each other within approx. pH=2units, the zero-crossover point of $d^2\Psi_o/dpH^2$ deviates from the values of affinity constants confirming the self-interactions of the reactive sites of amphoteric molecules.

References

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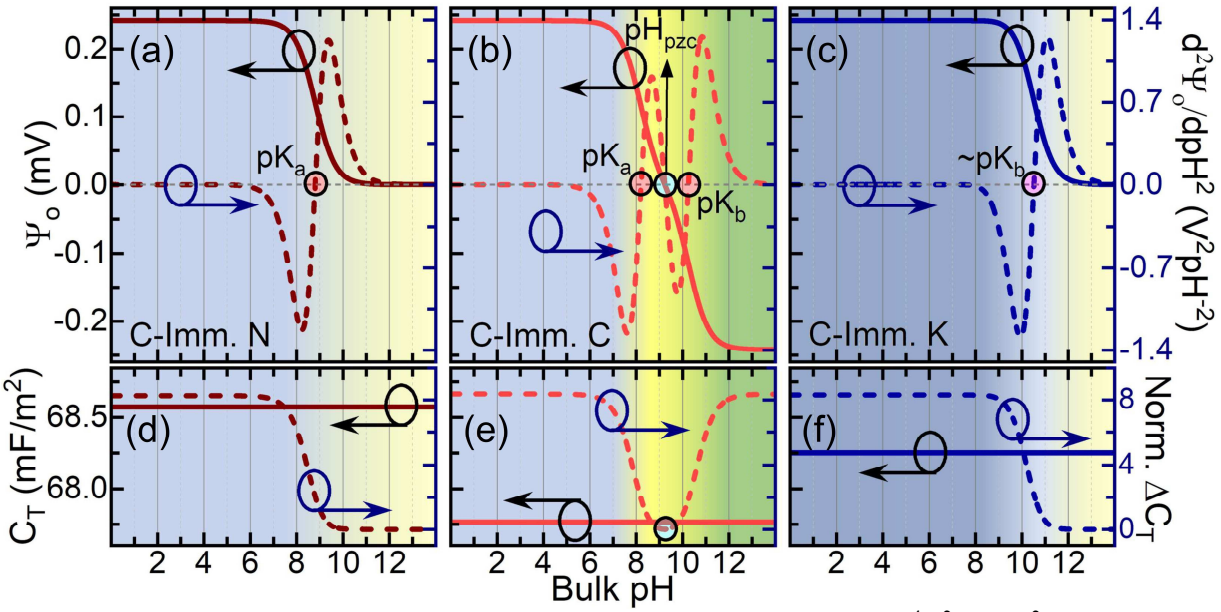

Figure 1. (a) to (c) Surface Potential (solid line) and 2nd Gradient of Surface Potential ($\times 10^{-4}$ $d^2\Psi_o/dpH^2$) (dashed line) for N, C and K amino acids, respectively (d) to (f) Total Capacitance (C_T) (solid line) and Normalized ΔC_T [$\times 10^{-6}$ (C_T-min(C_T))/(min(C_T))] (dashed line) of ISFET with respect to the pH for Carboxy-terminal immobilized amino acids for N, C and K, respectively. [Note: Calculated for electrolyte concentration = 0.001M and density = 10^{12} mol.cm^{-2}]

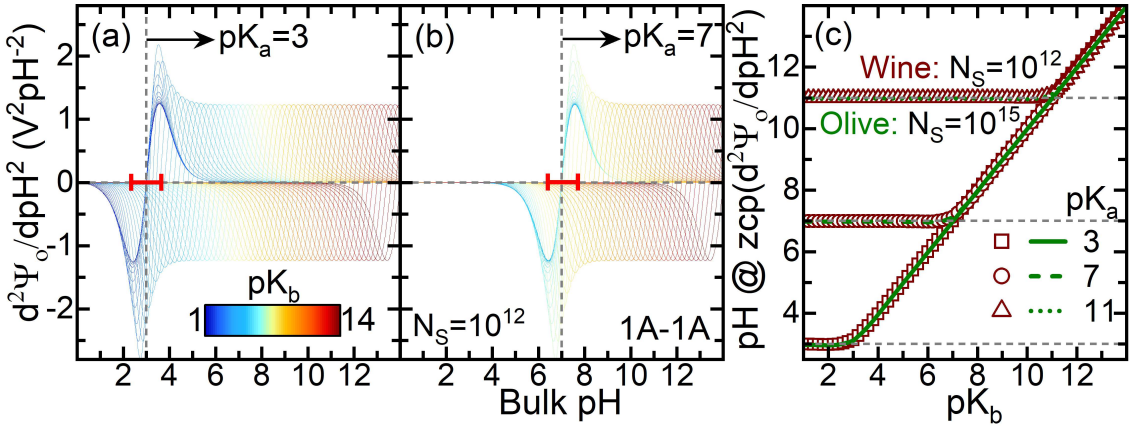

Figure 2. 2nd order Gradient of Surface Potential ($d^2\Psi_o/dpH^2$) of ISFET with respect to the pH for Carboxy-terminal immobilized Amino acid (example: Lysine) having two free amine reactive sites (one α-amine and one amine sidechain) for varying pK_b and fixed (a) pK_a=3 (b) pK_b=7 [Note: Calculated for electrolyte concentration = 0.001M] (c) Zero-crossover point (in terms of pH) of $d^2\Psi_o/dpH^2$ of ISFET with respect to the varying pK_b and fixed pK_a (3, 7 and 11) of Carboxyl-terminal immobilized Amino acid on the sensing surface of Electrolyte-Gated FinFET for different surface density (10^{12} and 10^{15} cm^{-2}).

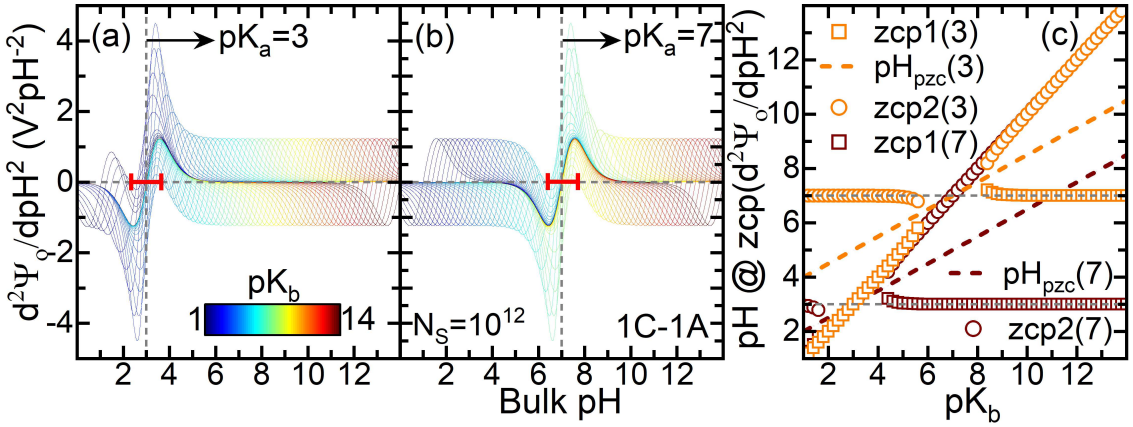

Figure 3. 2nd order Gradient of Surface Potential ($d^2\Psi_o/dpH^2$) of ISFET with respect to the pH for Carboxylic-terminal immobilized Amino acid (example: Cysteine) having one α-amine and one sulphur sidechain for varying pK_b and fixed (a) pK_a=3 (b) pK_b=7 [Note: Calculated for electrolyte concentration = 0.001M] (c) Zero-crossover points (in terms of pH) of $d^2\Psi_o/dpH^2$ of ISFET with respect to the varying pK_b and fixed pK_a (3 and 7) of Carboxyl-terminal immobilized Amino acid on the sensing surface of Electrolyte-Gated FinFET for surface density = 10^{12} cm^{-2}.