Interactive model for DNA specificity and selectivity and biosensor validation

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Abstract. Specific and selective detection of biomolecule has become major research quest of scientist community, most diseases are curable however, early specific detection and selective nature determine this capabilities, thus need rogue sensor specificity and selectivity testing. Sensor specificity/selectively largely depend on the robust validation approach adopted. This paper presents the interactive Model for DNA Specificity and Selectivity in Biosensor Validation. The partial charge induced due to hybridization of complementary ssDNAs caused a significant change in the conductance of sensor specific potential. The interactive model of inorganic and organic behaviour was calculated based on first principle. The partial charge due to ssDNA and dsDNA molecule was computed using molecular dynamics (MD) simulation. The results show that, the full and identification of compliment, mismatched with precise sequence of acid bonds with specific time response of 1016 and 1020 for 0.0095 ns, 0.008nS respectively. With this fast and accurate response, the model could be used for the biosensor validation.

Keywords: Bio sensor, DNA, Specific, Speciality, Validation.

1. Introduction
The general interactive model based on mathematical description to identify selective potential with binding sites attenuation of biosensor have become very important step in validating sensors [1-5]. The ability of validating sensor based on simulation to understand interaction between organics (DNA) and inorganic sensor will exactly tell the behavior of the sensor [6]. The sensor behavior changes based on changed in conductance due to induced partial charge across the sensor surface [7-11]. A comprehensive simulation framework is necessary to develop sensor behavior. Several approaches were shown from the literature using the finite element method and calculation of the partial charge due to DNA interaction using molecular dynamics simulator but in-depth presentation of various parameter still could not be found in literature. Thus, a robust approach based first principle is therefore quite to create benchmark where experimental sensors could be tested [12-17]. The approach adopted to realise this platform is mostly based on Molecular dynamic (MD). MD is powerful approach to tell what happen between organic and nonorganic elements. a simulators based on MD is used for DNA molecules was utilized here as well in this study. The DNA simulation with
exact code number are utilized, two ssDNA hybridization based induced partial charge was introduced. A complete simulation framework for an interaction between sensor and DNA is presented [18]. The effects of hybridization induced partial charge on the interaction between organic molecule (DNA) and inorganic biosensor was investigated through the simulation of the sensor electrical response. A strand based simulation of DNA using molecular dynamic simulation (MD). These two components DNA and Sensor are integrated to develop an overall simulation framework [19]. These simulations were done in three steps. Initially, sensor was simulated and tested without the counter biomolecule part (DNA) molecules. In the second step, the simulation of biosensor with probe ssDNA was performed. Due to the partial charge of ssDNA, the conductance of transducer was monitored. Finally, the third step involved hybridization between probe ssDNA and the target ssDNA molecules. In these steps, the partial charge induced due to hybridization of complementary ssDNAs caused a significant change in the conductance of on the sensor. The details computational approaches are presented in the next part.

2. Computational

The sensor parameters are presented in tables 1 to 4. The parametric elements together with physics and driving equations to the model are presented. The sensor is influenced by surface phenomena. As such, the geometry play very important role, thus, a cylindrical wire was designed a nanowire with a very small size which has a 15 nm radius was proposed. It is surrounded by a layer which has a thickness of 2 nm. A functional bio-interface layer surrounding the oxide layer has receptor biomolecules probe and a thickness of 5 nm. The last layer is referred to as an electrolyte of 80 nm width in which the whole system was immersed.

| Table 1. The PDE coefficients for Subdomain 1 according (El) |
|---------------------------------------------------------------|
| Property | Value | Description |
| Γ        | eps_el*ux+ eps_el*uy | Flux Vector |
| F        | Cmul*(Z*c3*u+(Z*c3*u)^3/3) | Source term |

| Table 2. The PDE coefficients for Subdomain 2 according(Fn) |
|---------------------------------------------------------------|
| Property | Value | Description |
| Γ        | eps_fn*ux+ eps_fn*uy | Flux Vector |
| F        | Cmul*(Z*c3*u+(Z*c3*u)^3/3) | Source term |

| Table 3. The PDE coefficients for Subdomain 3 according(O2) |
|---------------------------------------------------------------|
| Property | Value | Description |
| Γ        | eps_o2*ux+ eps_o2*uy | Flux Vector |
| F        | 0 | Source term |
Table 4. The PDE coefficients for Subdomain

| Property | Value | Description |
|----------|-------|-------------|
| $\Gamma$ | $\varepsilon Si^* u_x + \varepsilon Si^* u_y$ | Flux Vector |
| $F$ | $c_{add} + c_1(1 - c_3u + (c_3u)^2/2 - (c_3u)^3/6) + c_2(1 + c_3u + (c_3u)^2/2 + (c_3u)^3/6)$ | Source term |

The potential distribution in the extracellular medium described by the electrostatic form of the geometry conduction, using the electrostatic and the second PDE. The nonlinear differential equations describing the membrane behavior are coupled with the FEM solution, called Boundary Conditions. Also, coupling is achieved by setting the boundary conditions (BC). All boundaries of the sensor axon in the PDE subdomain are set as Neumann BCs; the normal component of the electric potential is zero. Boundary and interface conditions are specified. All boundaries of sensor in the PDE subdomain are included in the major interaction. In the electrostatics mode, two sets of boundary conditions were considered using different parameters of electric potential and electric shielding of boundary condition (BC), the boundaries are electric potential, and boundaries are electric shielding are used for boundary condition layers. The parameters values for different boundaries are formed. As there are four layers, and four boundaries including the boundaries between electrolyte and environment. However, for convenience, each boundary is divided into four equal parts. Thus, there are totally 16 boundaries on the sensor for complete active areas.

A finite element mesh was generated for the model geometry. It is important to judiciously determine the element size of the mesh generation. On the other hand, a coarse granularity will require less computational power, but at the expense of accuracy of the result. The final step of simulation SINWEFT is Mesh Generation. A tetrahedral mesh is used with a finer mesh around the wire and a coarser one in the external domain, this next part shows the result of the simulation.

3. Results and Discussions
A visualization software packages called Visual Molecular Dynamics (VMD) has been used for the 3D visualization of the data. PDB files have a list of atoms with their three-dimensional coordinates. Each atom has an index and a name. A collection of atoms is classified as shown in figure 1. VMD has a comprehensive graphical user interface for loading, visualization and modification of data.
In this step, the simulation partial charge of probe ssDNA was computed. The DNA sequence 5’ A-G-T-C 3’ is considered as probe ssDNA. In order to calculate the partial charge for this probe ssDNA, this ssDNA was first simulated using the molecular dynamic method with a suitable force field. The results were found by simulation, and thus topology file was obtained. This topology file contained various topological information including the partial charge of all the residues of ssDNA. From this topological file, the partial charge of the resinous along with their coordinate values were extracted and saved for later use in the interaction with nanowire biosensor. A snapshot of the topology file is shown.

The conductance of the silicon nanowire decreases because there is no partial charge of probe ssDNA. With the doping $10^{10}$, the conductance is 0.0095 nS, and the doing $10^{16}$ and $10^{20}$, the conductance is 0.006 nS and 0.008 nS, respectively. When probe ssDNA is immobilized into the biosensor nanowire, the conductance of silicon nanowire significantly increased. In this case, the conductance of the silicon nanowire at the doping level of $10^{10}$, $10^{16}$ and $10^{20}$ are 0.0095 nS, 0.008nS, and 0.02nS is presented, respectively. Moreover, from the different conductance of silicon nanowire shown in figure 2, higher conductivity at nanowire conductance affected by immobilized of partial charge dsDNA and decreasing the conductivity of nanowire without ssDNA is presented. The sensitivity of silicon nanowire is calculated to present sensitivity between silicon nanowire and ssDNA probe of partial charge with around 35%. Figure 2 shows the result of the interaction between silicon nanowire with the detection of single strand DNA probe of 5’ A-G-T-C 3’ immobilised. Moreover, the conductance of silicon nanowire is affected by ssDNA molecules. The result shows different conductance of silicon nanowire when simulated by itself. The second conductance is with ssDNA probe and shows a high conductance with applied DNA detection due to the partial charge DNA because the electron charge silicon nanowire is affected. Moreover, the calculation of conductance silicon nanowire between Si and immobilization using general equation is $G_{im} - G_{Si} = \text{conductance}$. The sensitivity equation used for the calculation between nanowire and immobilization is calculated by: $= \frac{G_{im} - G_{Si}}{G_{Si}} \times 100\%$. The result shows single strand DNA, affecting the conductance of silicon nanowire and the changes in the sensitivity of silicon nanowire, the calculation of the conductance of silicon nanowire after changes due to the effect of immobilization on the performance of nanowire, which indicates high values in the conductivity and changes in the sensitivity, compared with previous experimental study.

The estimated sensitivity is consistent with the previous and existing literature that solids symbols, and DNA detection are at higher single strand DNA probe concentrations. Since the average number of molecules on the surface varies with the bulk ssDNA concentration, the data are not used for comparison. Additionally, the single strand molecules are assumed to be at a distance of 2 nm from the
silicon nanowire surface, with the axis of DNA helix perpendicular to the semiconductor axis. Since the base pairs contribute to zero charge due to the consideration of the backbone of the DNA strands. The results revealed that simulation silicon nanowire at ion levels is higher, and there is an incremental change in conductance by increasing DNA single strand and reducing the length due to the electrostatic screening by the ions. That is caused by the efforts towards genome sequencing DNA using nanowire biosensors. Means indicates that it is very difficult to differentiate between sequences DNA because they have no difference in the number of base pairs in the sequence. It is possible to get a charge because DNA leads to the presence of phosphate ions in the backbone of single strand DNA but not because of the individual base pair. In this case, these results indicate the difference between DNA strands of similar length but show no difference in base pair sequences due to electrostatic considerations separately. Hence, in this case, the ion concentration of the solution is very high to ensure the conjugation between the negatively charged target and receptor strands (DNA strands due to the presence of phosphate ions in their backbone).

Figure 2. Hybridization dsDNA by using GROMACS simulation

A result and discussion about double strand DNA hybridization complementary target for creating the partial charge are presented above. However, the last section of result of target hybridization shows different results of creating the partial charges for the interaction with silicon nanowire. At the step of the computed partial charge for studying the effects of the partial charge on the conductance of silicon nanowire, the partial charge was computed for hybridization target dsDNA. The biosensor works based on the change in the nanowire conductance due to hybridization induced partial charge. This change in conductance can be computed from the simulation of the interaction of biosensor with DNA. dsDNA considered for this section is visualization snapshot of the simulation is shown below.
Figure 3 shows the occurrences of the partial charge at different residues of the dsDNA as small bright dots. These partial charges were calculated using molecular dynamic simulations and integrated into COMSOL based nanowire biosensor simulation. The final simulation results are shown in figure 3. The blue one represents the relationship between nanowire conductance and semiconductor doping concentration when none of the ssDNAs are presented. The black one represents the conductance of silicon nanowire when the conductance is affected by probe ssDNA. The red one represents the relationship between nanowire conductance and semiconductor doping concentration when hybridization induced partial charge of dsDNA affects the conductance of silicon nanowire.

4. Conclusion
The theoretical model which could be used to determine behavior of biosensor presented in this study. The work demonstrated, a model for the biosensor for DNA Specificity and Selectivity in Biosensor Validation. The partial charge induced due to hybridization of complementary ssDNAs caused a significant change in the conductance of sensor specific potential. The interactive model of inorganic and organic behaviour was calculated based on first principle. The partial charge due to ssDNA and dsDNA molecule was computed using molecular dynamics (MD) simulation.

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