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Enhancement of Biomolecular Mass Transport by Electrophoresis in Nanoscale Biosensors

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ABSTRACT

We discuss the importance of active biomolecular transportation in nanoscale biosensors. Simulation results based on finite element method show the effect of electrostatic field driven by molecular transportation, and indicate that active driving force is necessary for efficient biomolecular detection in sample solution with low target concentration. Our numerical model provides a guideline to design nanoscale biosensors by considering various design parameters such as electric field intensity, molecular concentration, and sensor size.

Keywords: Mass transport, Nanoscale biosensor, Electrophoresis, FEM analysis, Microfluidics

Introduction

Scaling down of biosensors using various nanoscale building blocks such as silicon nanowires and carbon nanotubes has drawn much attention due to its potential to implement high sensitive biosensors. High sensitive biosensor applications such as detecting a single virus attachment or low concentration DNA hybridization are demonstrated using nanowire field effect transistor and carbon nanotube biosensors, and other nanoscale detection schemes[1-7]. Miniaturizing the sensor generally increases the sensitivity for the signal transduction. The smaller sensors are, the higher the sensor sensitivity to the specific molecule becomes.

However, for the smaller sensors, the probability of the molecule finding the sensor decreases, which results in practical trade-offs between the sensitivity and the size of the biosensors[8]. If a molecule migrates to the sensor by diffusion only, time required for the molecule to diffuse to the sensor is not negligible in low molecular concentration. For example, it will take more than a day for the first molecule to find the sensor if the sensor is shaped as a 10 nm sphere at 1 fM molecular concentration[8]. Therefore active molecular transportation is important in nanoscale biosensors.

In this paper, we present an enhanced mass transportation model that shows the electrophoretic mass flux of the biomolecule to the nanoscale biosensor. The model includes the effect of active molecular transportation by electrophoresis various parameters such as molecular concentration, field intensity and the sensor size.

Results and Discussion

First, we present a mathematical model that describes the electrophoretic mass flux of the biomolecule to the nanoscale biosensor. Based on the fact that DNA-like biomolecules are negatively charged, we assume that the motions of the biomolecules are influenced by the diffusive force and the external electrostatic force generated from the sensor. Thus, mass flux can be stated from the superposition of these two different transport mechanisms. This is given by

$$j = -D\nabla C + \nu C \tag{1}$$

Where j is the mass flux, D is the diffusion constant, C is the concentration profile, and ν is the stationary migration velocity profile resulting from the electrostatic force. First term of the eq. (1) show the effect of diffusion, and second term represents the effect of electrostatic field acting on charged biomolecules. We incorporated it into the continuity equation for mass conservation, and this is given by

$$\frac{\partial C}{\partial t} = D\nabla^2 C - \nu\nabla C \tag{2}$$

In electrophoresis, molecular migration velocity is given by

$$\nu = \mu E \tag{3}$$

Where μ is the electrophoretic mobility of the molecule in certain buffer, and E is the electric field. If we know the concentration profile from the eq. (2) and eq. (3), we can determine the mass flux from the eq. (1). For biosensors to detect a certain molecule, the molecule should first accumulate on the sensor's surface. The accumulation quantity N is defined by

$$N(t)=\int_0^t \int_A j \cdot d\sigma d\tau \quad (4)$$

σ is a unit area of the sensor's surface, and t is the accumulation time[8].

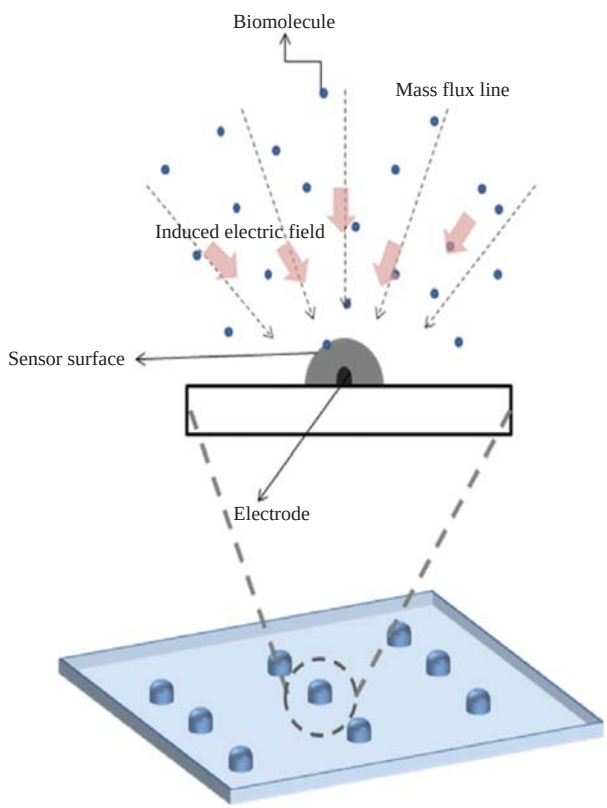

Figure 1. Schematic diagram of the biosensor and simulation setting. An electrode in the sensor generates electrostatic field. Added to the diffusive mass flux, it can enhance the mass transport effect through the sensor's surface.

For simulation, we assumed that sensors are hemispherical as described in Figure 1, which depicts our simulation condition in which, a nanoscale sensor is biased to pull the charged molecules electrophoretically. The boundary conditions pertinent to the simulation are as follows:

$$r=r_{surface},\ C=0 \quad (5)$$

$$r\rightarrow\infty,\ C=C_{bulk} \quad (6)$$

Boundary conditions (5) states that when molecules are adsorbed to the sensor's surface, every particle is gobbled up. We use numerical values of 20 base pair long single-stranded DNA, whose mobility is $3.0\times10^{-4}\,cm^2\,V^{-1}\,s^{-1}$, and diffusion constant is $1.52\times10^{-6}\,cm^2\,s^{-1}$ [9].

Exact analytical solution of eq. (2) with complex boundaries is usually hard to get. To get the estimated concentration profile, eq. (2) was solved numerically using finite element method platform. After obtaining the concentration profile, we get the mass flux described in eq. (1). We integrate net mass flux along the sensor's surface, and finally obtained accumulation quantity N at given accumulation time or vice versa.

Figure 2 shows the FEM simulation results of the cross section plot of the concentration profiles near the sensor and corresponding molecular traces. The electrostatic field induced mass flux through the sensor is far greater than the diffusion only case. Figure 3 shows that the electrostatic field affects the number of accumulated molecules on the sensor's surface. The inset of upper part of Figure 3 shows a sensor with 200 μm in diameter (typical probe size of DNA microarray fabricated by spotting) and the inset of lower part of Figure 3 shows a sensor with 20 nm in diameter.

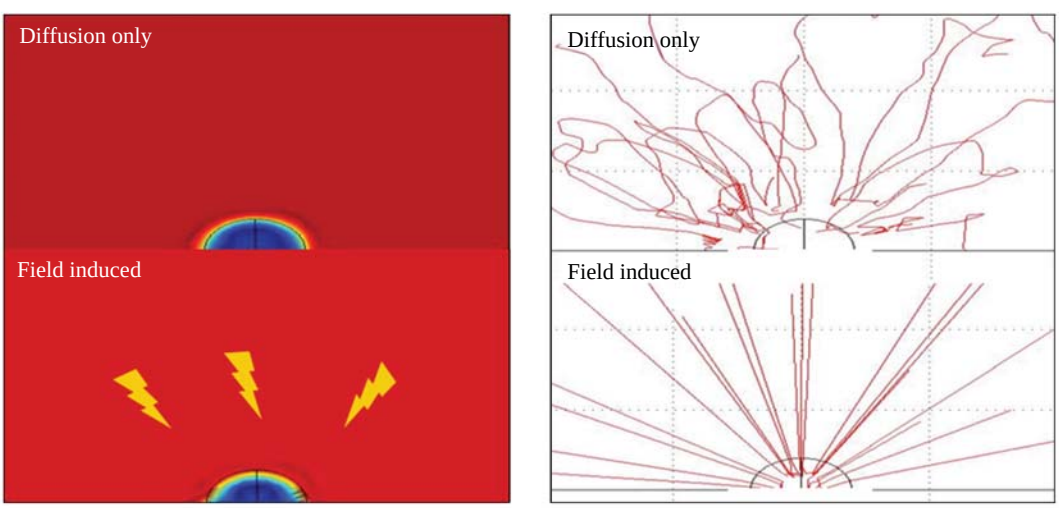

Figure 2. FEM simulation result: (left) Concentration profile (right) mass flux toward the hemispherical sensor.

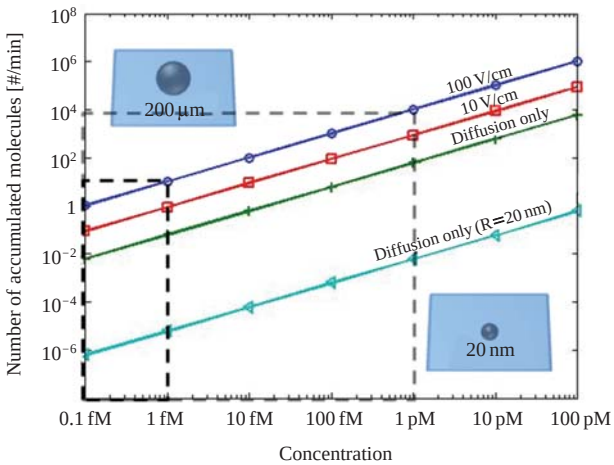

Figure 3. Comparison between passive mass flux and field-induced mass flux. In a 1 fM concentration for radius of 200 µm sensor, it is hard to detect single molecule in a minute. When using nanoscale sensors, the concentration condition should be over 1 pM for reasonable assay time.

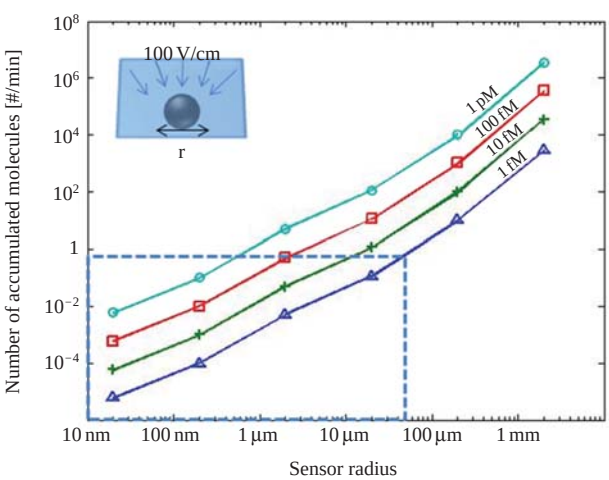

Figure 4. Effect of the sensor's size according to the concentration. In 1 fM concentration and 100 V/cm electrostatic field intensity, sensors with the radius of $< 50\,\mu m$ cannot detect a molecule in a minute. If the sensor size goes down to nanoscale, it takes too much time to detect a molecule.

If we detect every molecule adsorbs to the sensor's surface, approximately it takes an hour for the first molecule to encounter the sensor without electric biasing at a molecular concentration of 1 fM for 200 µm sensor. However when we apply the electrostatic field with intensity of 100 V/cm, it takes only a minute to accumulate a single molecule to the sensor's surface. If we want to detect a molecule at under femto molar concentration, electrostatic intensity over 100 V/cm is needed. We can verify the previous research that without any active driving force, nanoscale biosensors will be subject to picomolar-order detection limits for practical assay time[8]. For nanoscale sensor, without any active driving force, we cannot detect a molecule in minutes at molecular concentration lower that pM. This result indicates that active driving force enhances the mass transportation and it is especially important for nanoscale biosensor.

The effect of the sensor's size can be seen from the Figure 4. Fir electrostatic field intensity over 250 V/cm, the mobility for polyelectrolyte system is not stable because of the Joule heating[10]. Therfore, there is the limit of electrostatic field intensity, and we cannot apply electrostatic field as much as we want. The inset of Figure 4 shows the model of the sensor and applied electrostatic field intensity of 100 V/cm. The net mass flux through the sensor is affected by the sensor's radius. Below 50 µm radius at 1 fM molecular concentration, there is no accumulated molecule within 1 minute even with strong electrostatic force. For the sensor with radius 500 nm, there is no accumulated molecule in a minute under 1 pM concentration. Therefore it is important to consider the target concentration, size of the sensor, and the field strength together and to understand the limit of the mass transportation in the sensor designing process.

Conclusions

There are many types of biosensors such as surface Plasmon resonance based biosensor, microarray biosensors, nanowire biosensors, etc. When we try to design biosensors, we have to select a certain type of sensor considering many performance factors such as sensitivity, molecular concentration, reasonabl assay time, pH, ionic strength, temperature, etc. In biologically relevant media, pH and ionic strength plays an important role to determine mobility and diffusion constant, especially for electrophoretic molecular guidance[10,11]. What remains to be determined by future research is the effect of the other performance factors. Furthermore, it is necessary to compare between many types of the sensors, and find out advantages and disadvantages of each sensor at specific circumstances.

In conclusion, we have shown that the mass transport effects in the biosensors can be enhanced by active driving force, and the enhancement of molecular transportation is shown quantitatively. We expect that our result can be applied to high-sensitive biosensor design process.

Acknowledgements

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