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Research Paper

Electrothermal effect on the immunoassay in a microchannel of a biosensor with asymmetrical interdigitated electrodes

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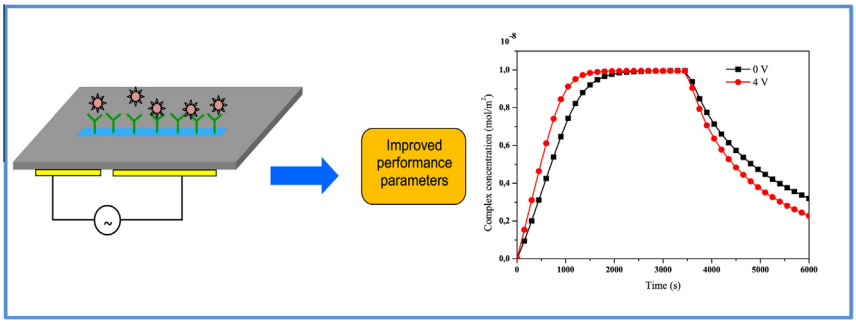
HIGHLIGHTS

- AC electro-thermal flow and heat generation have been studied.
- The temperature boundary condition influences significantly the binding rate.
- Highest electrical conductivity causes the stronger electrothermal flow.
- Lower substrate thermal conductivity raises the binding rate.

GRAPHICAL ABSTRACT



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ABSTRACT

In this paper, we study the AC electrothermal (ACET) effect on the binding reaction of immunoassays which a ligand (anti-C-reactive protein) immobilized on a microchannel wall specifically binds analyte (C-reactive protein (CRP)) flowing through a configuration of a microchannel with asymmetrical planar electrode pairs. The Navier–Stokes equations coupled with the Laplace and energy equations, the Fick's second law in convection–diffusion coupled with the first order Langmuir adsorption model are used. The set of equations is solved in a two-dimensional configuration using the finite element method. Three cases of the thermal boundary conditions are investigated to study the effect of the temperature field on the binding reaction efficiency. The electrical conductivity of the buffer solution, the thermal conductivity of the base material and the surface reaction length are also discussed in this work. The simulation results show that the heterogeneous immunoassay is improved when the external surfaces of the cover and the substrate are kept at a constant temperature. For the best case studied in this work, the enhancement factors of the binding curve can be raised up to 3.46 and 2.84 for the association and dissociation phases, respectively, with 4 V_{rms} applied voltage and operating frequency of 100 kHz and electrical conductivity of 0.01 S/m.

1. Introduction

Microfluidics-based biosensors and biochips have given impetus to develop immunoassays, protein separation, DNA sequencing and tremendous applications in life sciences and medical diagnosis [1–3]. Heterogeneous immunoassays, is a powerful biomedical diagnostic tool based on the interaction between free analyte

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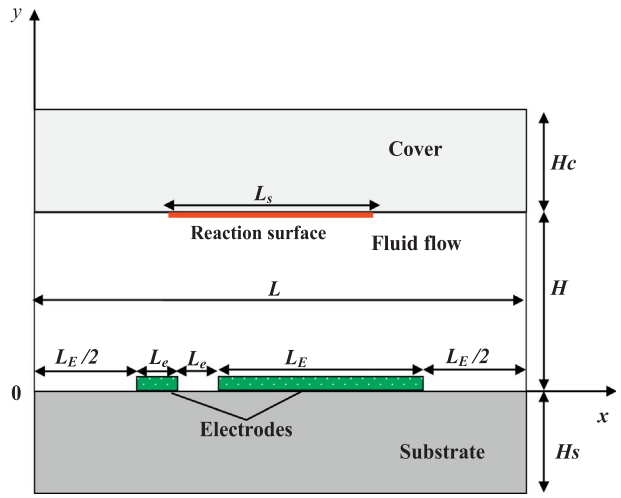

Fig. 1. Geometry of the computational domain.

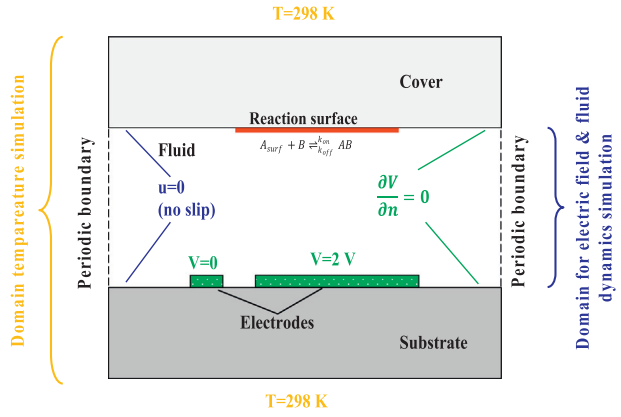

Fig. 2. The numerical simulation space assigned boundary conditions for the electrical, temperature, fluid velocity, convection–diffusion and the kinetic reaction models.

molecule and immobilized ligand receptor. The fluid containing a small concentration of antigen and flows through the microfluidic channels which will make a binding reaction with the immobilized ligands at the sensing zone. The surface plasmon resonance (SPR) sensor [4,5], the quartz crystal microbalance (QCM) sensor [6] and the impedance based sensor [7] are the most commonly used systems for detecting and monitoring the biomolecules. A problem that arises in these microdevices concerns the transport of the liquid samples and other solutions in the biochip, which are very small dimensions and the flow is always laminar and lacking turbulence at the microscale. In addition, the biomolecules are usually having small diffusion coefficients which take a longer time to transport by convection and diffusion to the reaction surface. The slower mass transport of the analyte to the sensitive membrane which restrain the whole kinetic reaction and it usually causes the formation of a diffusion boundary layer [8]. Subsequently, it limits the detection time of the biosensors and its performances [9–11].

Recently, a wide research experimental and theoretical has been devoted to overcome this problem and to develop technique to enhance mixing in microfluidics devices [12–16]. AC electrokinetic (ACEK) is one of the most promising techniques used to enhance mixing in microfluidic systems and it can be classified into three phenomena, i.e. AC electroosmosis (ACEO), AC electrothermal (ACET), and dielectrophoresis (DEP) [17–19]. The DEP is used to manipulate particles, focus DNA and separate cancer cells from blood [20]. ACEO has been utilized for pumping fluids having low conductivity and under low applied field frequencies (below 100 kHz) and it is insignificant in fluids with high electrical conductivities (i.e. 1 S/m) such as biological fluids and many solution buffers [21]. The AC electrothermal effect (ACET) has been tremendously used in the past few years in several researches for biological applications [21–25]. The ACET effect is influential at higher frequency (above 100 kHz) in a high-conductivity solution (above 0.002 S/m) [26]. Feldman et al. [21] have demonstrated through experiment and numerical study using a biotin-streptavidin heterogeneous assay, in which biotin is immobilized, and fluorescently-labeled streptavidin issuspended in a high conductivity buffer (σ = 1 S/m) that electrothermal microstirring can be used to improve heterogeneous binding by up to a factor of 9 using a 10 V_{rms} applied potential. Sigurdson et al. [22] have investigated experimentally and numerically the electrothermal fluid motion and have predicted that the binding rate of heterogeneous immunoassays can be increased by a factor 7 by applying 6 V_{rms} applied voltage. Huang et al. [24,25] performed in their studies two and three dimensional full time scales finite element simulation on the binding reaction kinetics of two proteins (CRP) and immunoglobulin G (IgG). The binding rate of heterogeneous immunoassays for CRP can be increased by a factor 2 by applying 15 V_{rms} applied voltage. The ACET flow exists in a much wider range experimentally and numerically in several researches for biological applications. However, these studies are still missing the thermal point of view. The present paper encompasses the thermal consideration which is very interesting in the biological applications.

In the present study, we will investigate the effect of the electrothermal flow (ACET) on the binding reaction efficiency of CRP in the configuration of a microchannel with asymmetrical interdigitated electrodes. Three cases of the thermal boundary conditions are investigated to study the temperature field effect on the performance biosensor. The effect of some important parameters such as the electrical conductivity of the buffer solution, the thermal conductivity of the base material, as well as the surface reaction length, that control the immunoreaction in the microfluidic biosensor and its response time are discussed. The Navier stokes equations is coupled with Laplace equation and the energy equation are solved using the finite element method to estimate the electrothermal flow and investigated its effect on the binding reaction of the biosensor.

2. Theoretical formulation

We aim in this study to investigate the electrothermal flow on the binding reaction kinetics of analyte-ligand (CRP-anti-CRP) in a microchannel with asymmetrical interdigitated electrodes.

2.1. Binding reaction analyte-ligand

The analyte diffused fraction toward the sensitive membrane reacts with the antibody ligand immobilized on the reaction surface. The binding reaction gives rise to a complex *AB*:

$$A_{surf} + B \rightleftharpoons k_{off}^{k_{on}} AB$$

where $[A]_{surface}$ is the analyte concentration at the surface, $[B]$ is antibody concentration, $[AB]$ is the complex concentration. The association and dissociation rate constants are respectively denoted by k_{on} and k_{off}.

We assume that the antibodies *B* and the complex *AB* are immobilized on the surface and do not diffuse.