

## **BIOSENSOR PERFORMANCE ENHANCEMENT THROUGH AC ELECTROKINETICS**

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### **ABSTRACT**

Biosensors can be limited in both response time and sensitivity by the diffusion of analyte to a sensing surface. AC Electric Fields applied in biosensor microchannels can generate motion of fluid and of suspended particles. It is proposed that biosensor response be improved by using AC electrokinetically-driven microscale fluid motion to enhance analyte motion towards immobilized ligands. Numerical suggest that 14 V rms applied to electrodes strategically placed opposite a narrow binding region can increase binding in the first few minutes by a factor of five. Optimization of the electrode geometry and placement can render this technique useful for a large variety of microfluidic sensors.

**Keywords: electrokinetics, immunoassay, micromixer**

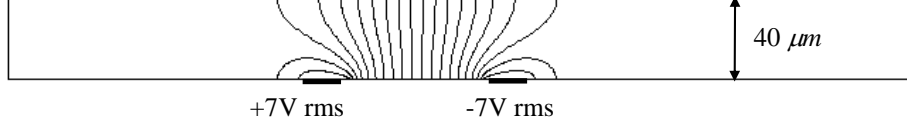
### **1. INTRODUCTION**

In heterogenous immunosensors a ligand (e.g. an antibody) immobilized within a microchannel captures for detection analyte (antigen) flowing through the channel. Detection of the antigen then can be realized through a number of methods [1]. In many cases, (good surface immobilization; strong binding affinity; larger sample volume) the response time of the sensor is limited by diffusion of the analyte to the sensor surface. If the cross-stream transport can be increased, so can the response of the sensor.

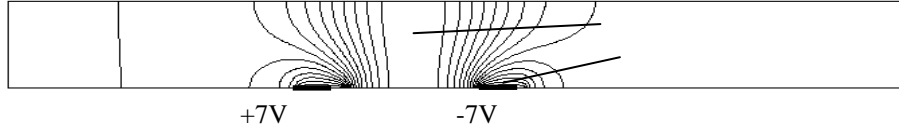
AC Electrokinetics refers to induced particle and/or fluid motion resulting from externally applied AC electric fields, and can be classified into three broad areas: dielectrophoresis (DEP), electrothermal forces, and AC electroosmosis. It is predicted that of these, electrothermally generated flow will be the most effective for the transport enhancement of small (~5 nm) proteins within a microchannel. Electrothermal flow results from non-uniform temperature fields creating conductivity and permittivity gradients, which interact with the electric field to generate flow patterns near the electrodes. Electrothermal flow is proposed to create microscale stirring, thereby enhancing transport of analyte to the binding region of a biosensor.

### **2. NUMERICAL SIMULATIONS: ELECTROTHERMAL FLOW**

The finite element packages CFD-ACE+ (CFD Research Corp, Huntsville, AL) and FEMLAB (COMSOL AB, Stockholm, Sweden) were used to simulate electrothermally



**Figure 1.** 2-D simulation of quasi-static electric potential contours in microchannel.



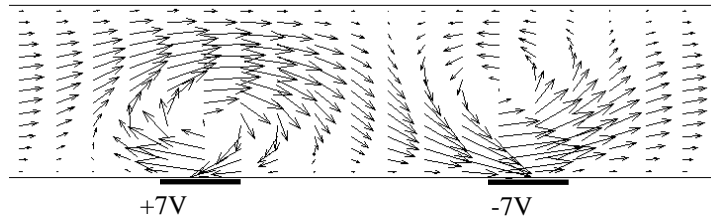
**Figure 2.** Temperature field generated by field in Figure 1.

induced flow and subsequent enhanced binding in the cavity. First, the quasi-static potential field produced by two electrodes along the cavity wall subjected to an AC ( $\sim 100\text{kHz}$ ) field is calculated (Fig. 1). Ignoring unsteady effects, and balancing Joule heating with thermal diffusion, a non-uniform temperature field is calculated (Figure 2). Gradients in temperature produce gradients in permittivity and conductivity in the fluid. These variations in electric properties produce gradients in charge density and perturb the electric field. Assuming the perturbed electric field is much smaller than the applied electric field, and that advection of electric charge is small compared to conduction, the time-averaged electrothermal force per unit volume for a non-dispersive fluid can be written as [2]

$$\vec{F}_{ET} = -0.5 \left[ \left( \frac{\nabla \sigma}{\sigma} - \frac{\nabla \varepsilon}{\varepsilon} \right) \vec{E}_{rms} \frac{\varepsilon \vec{E}_{rms}}{1 + (\omega\tau)^2} + 0.5 |\vec{E}_{rms}|^2 \nabla \varepsilon \right] \quad (1)$$

The first term on the right hand side of Eq. (1) is the Coulombic force, and is dominant at low frequencies. The second term is the dielectric force, and is dominant at high frequencies. The crossover frequency scales inversely with the charge relaxation time of the fluid, and typically occurs at around several MHz.

The electrothermal force shown in Eq. (1) is a body force on the fluid. The motion of the fluid can be determined by solving the Stokes' equation for zero Reynolds number fluid flow, and is shown in Figure 3. The velocity of the ETF is of order  $300 \mu\text{m/s}$ , and characterized by a pair of counter rotating vortices. The fluid is convected with small eddy motions, which may effectively stir the analyte. If antibodies have been immobilized on the channel wall in a region of increased flow, these eddy motions will transport antigen to the antibody binding region.



**Figure 3.** 2-D simulation of electrothermally enhanced velocity field in microchannel (center section only to show detail).  $100 \mu\text{m/s}$  pressure driven flow is enhanced by electrothermal flow generated by two electrodes along channel bottom. Electrothermal velocity is of order  $300 \mu\text{m/s}$ .

### 3. NUMERICAL SIMULATIONS: BINDING ENHANCEMENT

We now investigate the effect these flow patterns may have on the binding response of an assay in which antibody has been immobilized along a short length of the microchannel wall. Velocity field shown in Figure 3 suggests the most effective location of the binding surface be on the wall opposite the first electrode. The convective scalar equation subject to a first order binding boundary condition at the binding surface (equations given in [3]) predicts the suspended concentration of antigen within the microchannel. Figure 4a shows the binding nondimensionalized by the immobilized antibody concentration ( $R_T=1.7 \text{ nM cm}$ ) for non-enhanced (0V) as well as enhanced (7V, 14V) microchannel flow. Often these assays are performed in a microarray rather than flow-through format. Figure 4b therefore shows binding enhancement predictions for a similar geometry with zero net flow. In both cases, several factors increase in binding are predicted in the first 100 seconds.

### 4. CONCLUSIONS

By designing a microchannel electrode system that takes advantage of electrothermal effects, cross-stream transport of an antigen and hence binding can be enhanced. Numerical simulations here predict factors of 2~8 improvement; with electrode and heat transfer optimization, an order of magnitude increase in binding rate may be achieved. This enhancement technique can be applicable to a wide variety of assay formats.

### 5. ACKNOWLEDGEMENTS

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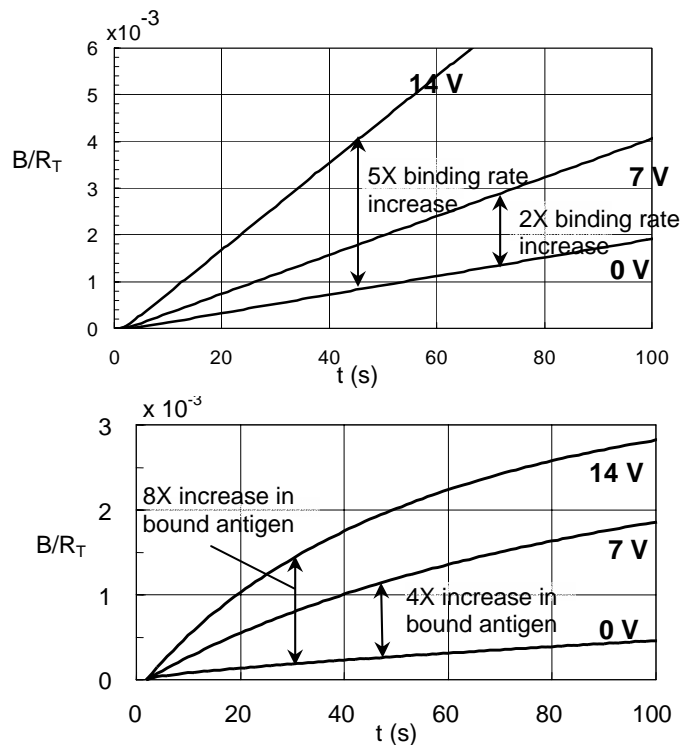


Figure 3: Numerical simulation of normalized bound antigen concentration, (a) in  $40 \mu\text{m}$  microchannel with inlet channel flow rate averaging  $100 \mu\text{m/s}$ . With  $7\text{V}$  applied rms voltage, the binding rate is about double the non-enhanced binding rate. With  $14\text{V}$  rms applied, the binding rate jumps to 5 times the non-enhanced rate. (b) in microcavity enhancement, with zero net flow. The differences in the two curves show an increase in binding rate which yields a factor of 4 higher binding for  $7\text{V}$  and a factor of 8 higher binding after 30 seconds for  $14\text{V}$  applied root-mean square potential. The binding improvement for the  $14\text{V}$  case decreases to around 6 X after 100 seconds: the binding is no longer completely transport-limited. These results suggest that electrothermally induced flow can significantly improve immunoassay performance by increasing binding rates.

## 6. REFERENCES

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