Concentration Gradient Immunoassay II. Supplemental Information

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ABSTRACT

A finite element model of novel immunoassay – the concentration gradient immunoassay (CGIA)[1] – was developed. The governing equations, initial conditions, and boundary conditions for the model which was solved in COMSOL® are presented in detail. The model solves the Poisson and steady-state Navier-Stokes equations to describe the fluid flow in the microchannel. The convection-diffusion and surface reaction equations were solved simultaneously and describe the transport of the antibody, analyte, and antibody-analyte complex in solution and the binding reaction of the antibody to the immobilized analyte. A pseudo-3d model describes the assay from the inlet to 22 mm downstream and uses the Poisson equation to solve the velocity profile. A 3d model simulates the assay in the binding area (see Figure 1 in the primary manuscript).

Table S-1. List of variables.

Variable	Description
c_s (moles m^{-2})	surface concentration of bound antibody
c_{Ab} (M)	concentration of antibody in solution
c_{Ag} (M)	concentration of analyte in solution
$c_{Ag\text{-}Ab}$ (M)	concentration of antibody-analyte (complex) in solution
c_{Ab0} (M)	initial concentration of antibody in solution
c_{Ag0} (M)	initial concentration of analyte in solution
$c_{Ag\text{-}Ab0}$ (M)	initial concentration of antibody-analyte (complex) in solution
c_{s0} (moles m^{-2})	initial surface concentration of bound antibody
$c_{Ag\ 22\ mm}$ (M)	concentration of antigen 22 mm downstream of inlet
$c_{Ab\_22\ mm}$ (M)	concentration of analyte 22 mm downstream of inlet
$c_{Ag\text{-}Ab\_22\ mm}$ (M)	concentration of antibody-analyte complex 22 mm downstream of inlet
k_{ads} (s^{-1})	binding rate of an antibody from solution to the surface
k_{des}(M^{-1}s^{-1})	dissociation rate of an antibody bound to the surface
θ (moles m^{-2})	available antibody binding sites per unit area
θ_0 (moles m^{-2})	total number of initial antibody binding sites per unit area
p (kg m^{-1} s^{-2})	pressure
x_s (m)	characteristic length (the depth of channel)
u (m s^{-1})	velocity in x-dimension
u_s (m s^{-1})	characteristic velocity (average velocity)
u_0 (m s^{-1})	parabolic inlet velocity for 3d model solved in pseudo-3d mode
v(m s^{-1})	velocity in y-dimension
w(m s^{-1})	velocity in z-dimension
ρ (kg m^{-3})	density
μ (kg m^{-1} s^{-1})	viscosity
D (m^2 s^{-1})	diffusion coefficient

A) Poisson equation

Solves the pseudo-3d velocity.

$-\nabla \bullet (\nabla \boldsymbol{u}) = \left(\frac{\partial p}{\partial x}\right) / \mu$	Eqn(1)

B) Navier-Stokes Equation[2]

Navier-Stokes equation*	$\rho \frac{\partial \boldsymbol{u}}{\partial t} + \rho \boldsymbol{u} \bullet \nabla \boldsymbol{u} = -\nabla p + \mu \nabla^2 \boldsymbol{u}$	Eqn(2)
Reynolds number	$\mathrm{Re} = \frac{\rho u_s x_s}{\mu}$	Eqn(3)

* At this size scale, gravitational effects are negligible and the gravity term drops out of the Navier-Stokes equation.

Boundary conditions			
Wall	Slip plane	Inlet	Outlet
$\boldsymbol{u} = 0$;	$\boldsymbol{n} \bullet \boldsymbol{u} = 0$;	$\boldsymbol{u} = u_0$;	Normal outflow; v=0, w=0;

C) Convection-diffusion equations governing reaction and transport in the solution

Reaction between antibody and analyte in solution

$c_{Ab} + c_{Ag} \underset{\mathrm{k_{off}}}{\overset{\mathrm{k_{on}}}{\Leftrightarrow}} c_{Ab-Ag}$	Eqn(4)

Convection-diffusion equations for each species[2]

$\frac{dc_{Ab}}{dt} + \nabla \bullet (-D \nabla c_{Ab} + c_{Ab} \boldsymbol{u}) = k_{off} c_{Ag-Ab} - k_{on} c_{Ab} c_{Ag}$	Eqn(5)
$\frac{dc_{Ag}}{dt} + \nabla \bullet (-D \nabla c_{Ag} + c_{Ag} \boldsymbol{u}) = k_{off} c_{Ag-Ab} - k_{on} c_{Ab} c_{Ag}$	Eqn(6)

$$\frac{dc_{Ag-Ab}}{dt}+\nabla\bullet\left(-D\nabla c_{Ag-Ab}+c_{Ag-Ab}\boldsymbol{u}\right)=k_{on}c_{Ab}c_{Ag}-k_{off}c_{Ag-Ab}$$	Eqn(7)

Peclet number for each species^2

$$Pe_{Ab}=\frac{x_s u_s}{D_{Ab}}$$	Eqn(8)
$$Pe_{Ag}=\frac{x_s u_s}{D_{Ag}}$$	Eqn(9)
$$Pe_{Ag-Ab}=\frac{x_s u_s}{D_{Ag-Ab}}$$	Eqn(10)

Initial conditions for pseudo-3d model (at inlet of the device)		
$c_{Ab0}=X\,*$	$c_{Ag0}=Y\,*$	$c_{Ag-Ab0}=0$

*where X and Y are arbitrary concentrations.

Boundary conditions for pseudo-3d model	
	Wall/Plane of symmetry
Antibody	$\boldsymbol{n}\bullet(-D\nabla c_{Ab}+c_{Ab}\boldsymbol{u})=0$
Analyte	$\boldsymbol{n}\bullet(-D\nabla c_{Ag}+c_{Ag}\boldsymbol{u})=0$
Antibody-Analyte complex	$\boldsymbol{n}\bullet(-D\nabla c_{Ag-Ab}+c_{Ag-Ab}\boldsymbol{u})=0$

Initial conditions for the 3d model		
$c_{Ab0}=0$	$c_{Ag0}=0$	$c_{Ag-Ab0}=0$

Boundary conditions for the 3d model				
	Wall/Slip plane	Inlet	Outlet	Binding Surface
Antibody	$\boldsymbol{n} \bullet (-D\nabla c_{Ab} + c_{Ab}\boldsymbol{u}) = 0$	$c_{Ab} = c_{Ab\,22\,mm}$	$\boldsymbol{n} \bullet (-D_{Ab}\nabla c_{Ab}) = 0$	$\boldsymbol{n} \bullet (-D\nabla c_{Ab} + c_{Ab}\boldsymbol{u}) = N_0$; $N_0 = -k_{ads}c_{Ab}(\theta_0 - c_s) + k_{des}c_s$
Analyte	$\boldsymbol{n} \bullet (-D\nabla c_{Ag} + c_{Ag}\boldsymbol{u}) = 0$	$c_{Ag} = c_{Ag\,22\,mm}$	$\boldsymbol{n} \bullet (-D_{Ag}\nabla c_{Ag}) = 0$	$\boldsymbol{n} \bullet (-D\nabla c_{Ag} + c_{Ag}\boldsymbol{u}) = 0$
Antibody-Analyte complex	$\boldsymbol{n} \bullet (-D\nabla c_{Ag-Ab} + c_{Ag-Ab}\boldsymbol{u}) = 0$	$c_{Ag-Ab} = c_{Ag-Ab\,22\,mm}$	$\boldsymbol{n} \bullet (-D_{Ag-Ab}\nabla c_{Ag-Ab}) = 0$	$\boldsymbol{n} \bullet (-D\nabla c_{Ag-Ab} + c_{Ag-Ab}\boldsymbol{u}) = 0$

D) Surface reaction

Dimensional form of the reaction equation is described in the primary manuscript.

Initial conditions	
$\theta_0 =$ 1 binding site every 25 nm^2	$c_{s0} = 0$

REFERENCES

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