
Modeling Chemical Reactions

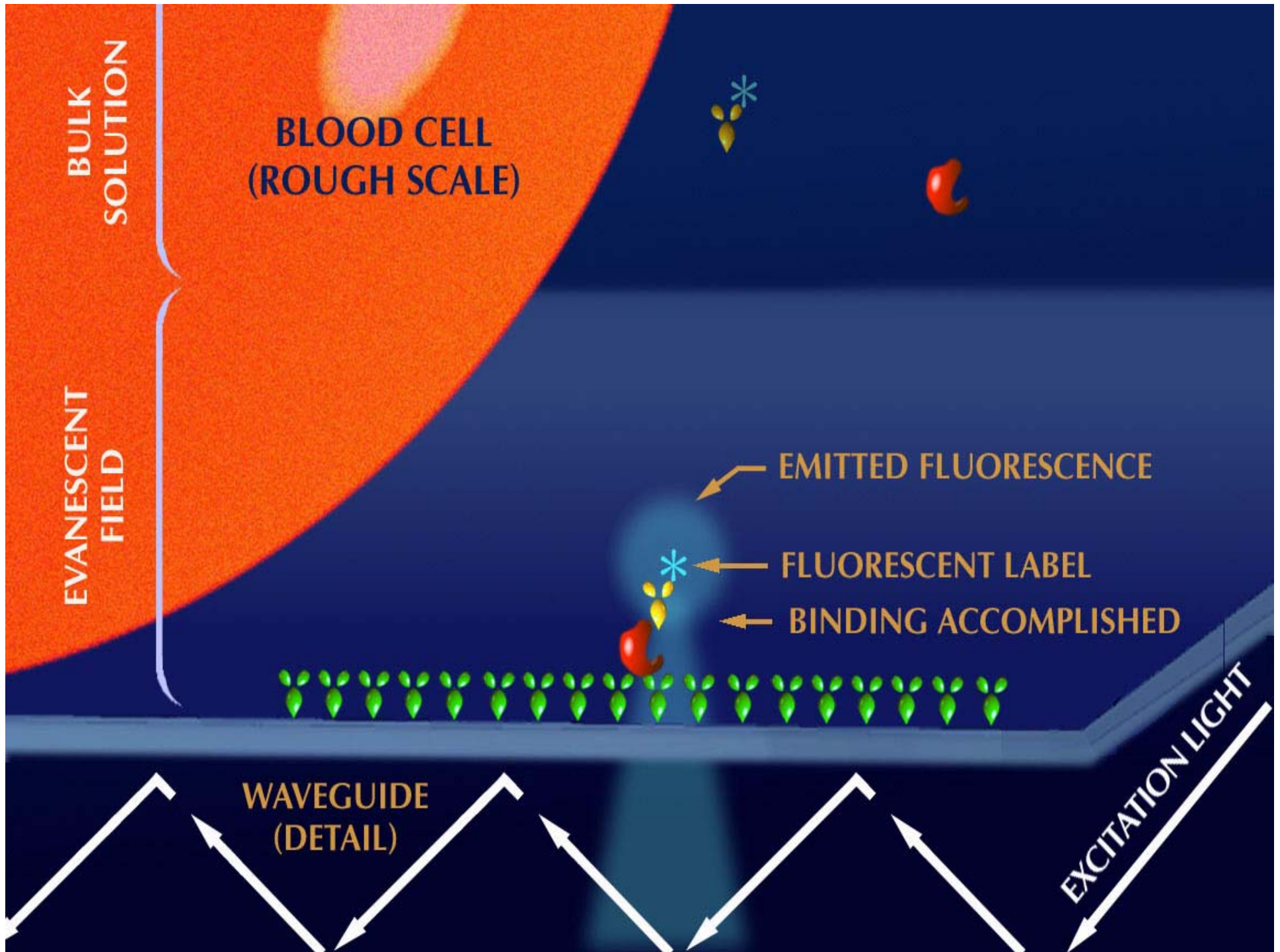
w/ Applications to Immunoassays and DNA Hybridization

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LifeLite[™] Reagent System (BioCentrex)





Scalar Transport and Reaction Kinetics

**Bulk
Concentration**

$$\frac{\partial c}{\partial t} + \vec{u} \cdot \nabla c = D \nabla^2 c + R_v$$

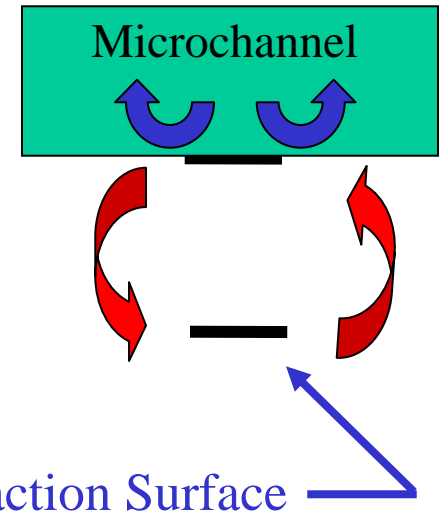
**1st Order
Heterogeneous
Reaction**

$$\frac{\partial B}{\partial t} = k_{on} c (R_T - B) - k_{off} B$$

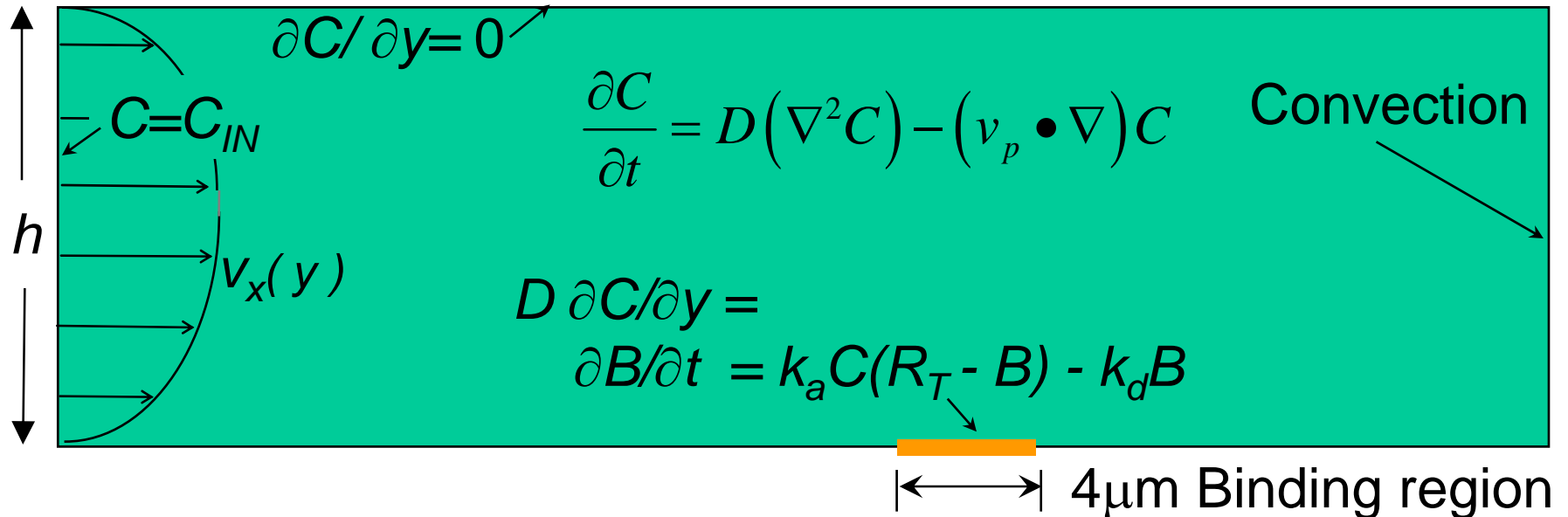
**Matching
Condition**

$$\underbrace{\frac{\partial B}{\partial t}}_{\text{Reaction Rate}} = -D \underbrace{\frac{\partial c}{\partial n}}_{\text{Diffusive Flux}}$$

Reaction Rate Diffusive Flux



Binding Model Applied to Microchannel Flow



Dependent Variables

$c(x, y, t)$: freestream antibody concentration

$B(x, t)$: bound antibody concentration

Parameters

C_{IN} Input Concentration

R_T : Immobilized antibody conc.

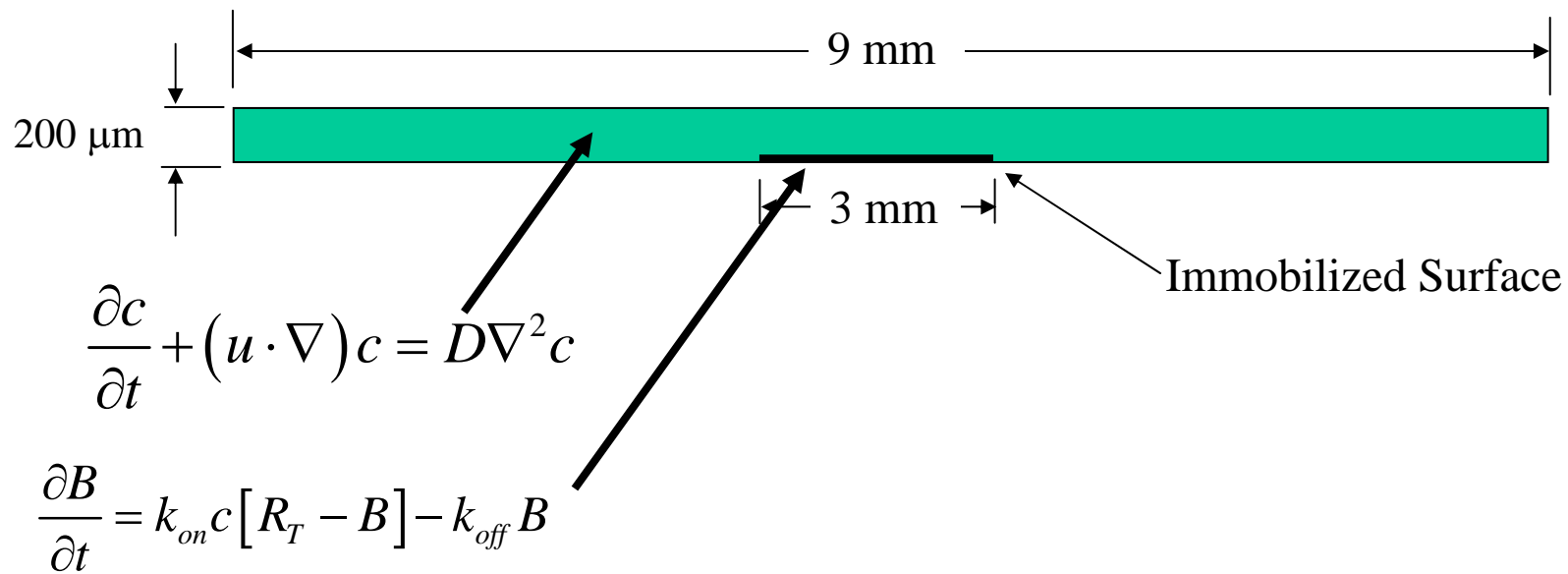
k_{on} , k_{off} : on & off rate constants

D : Particle diffusivity

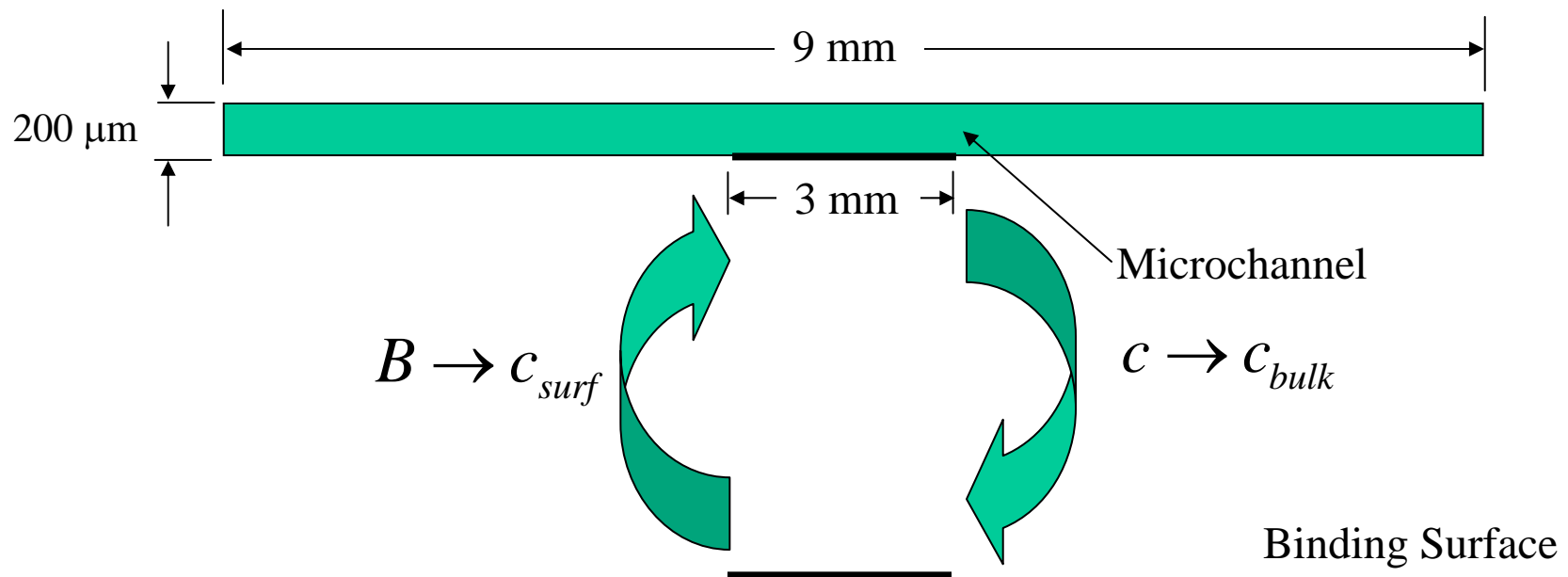
$V_x(y)$: Velocity profile

h : channel height

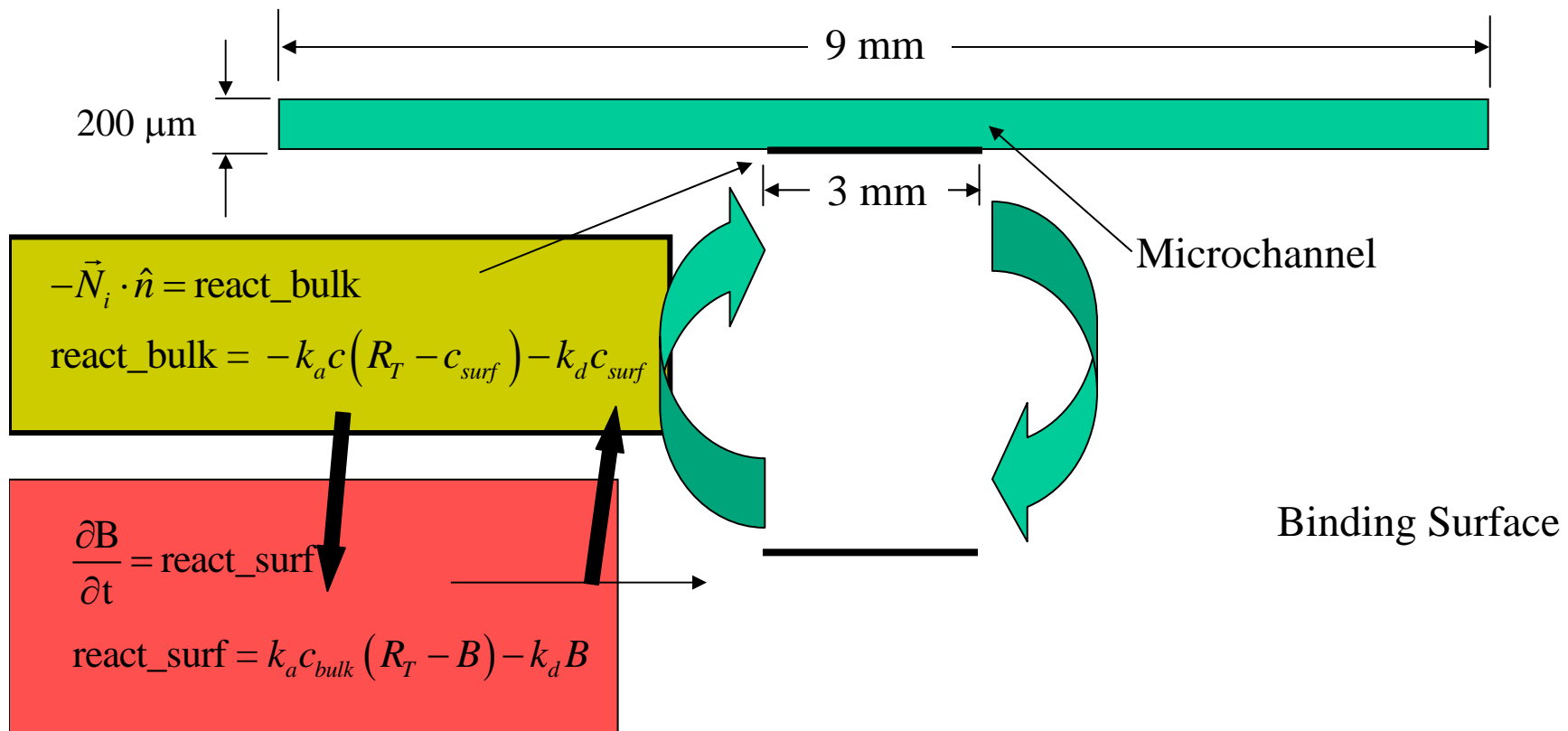
Simulation of Microchannel Binding (Full scale)



Microchannel Binding – Simulation Setup

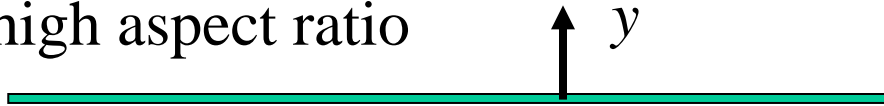


Microchannel Binding – Simulation Setup



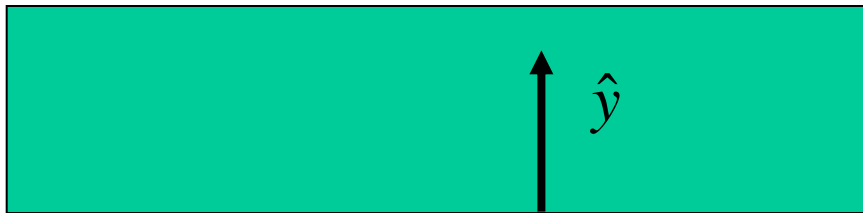
Large Aspect Ratio Channels (anisotropic diffusion)

- Stretch one coordinate so that channel does not have a high aspect ratio



- Stretch the coordinate

$$y = \alpha \hat{y}$$

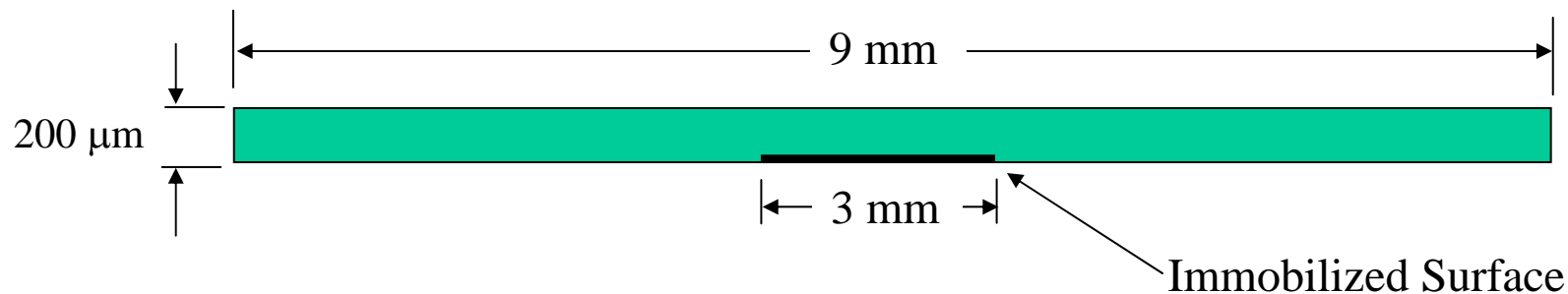


$$\frac{\partial c}{\partial t} + u \frac{\partial c}{\partial x} = \left[D \frac{\partial^2}{\partial x^2} + \frac{D}{\alpha^2} \frac{\partial^2}{\partial \hat{y}^2} \right] c$$

- Can simulate in Femlab using

$$\vec{\vec{D}} = \begin{bmatrix} D & 0 \\ 0 & D/\alpha^2 \end{bmatrix}$$

Simulation of Microchannel Binding (Full scale)



$$\frac{\partial c}{\partial t} + (u \cdot \nabla) c = D \nabla^2 c$$

Scalar concentration in fluid bulk

$$\frac{\partial B}{\partial t} = k_{on} c [R_T - B] - k_{off} B$$

First order binding rate kinetics of functionalized surface

Immobilization Parameters

Troponin

$$\left\{ \begin{array}{l} R_T = 2e16 \text{ molecules / m}^2 \times \frac{1 \text{ mol}}{6.02e23 \text{ molecues}} \times \frac{1e-3 \text{ m}^3}{1 \text{ liter}} = 3.32e-11 \text{ molar} * m \\ k_{on} = 6e7 \text{ L}/(\text{mol-min}) = 1e6 \text{ L}/(\text{mol-s}) \\ k_{off} = 6.00e-2 \text{ min}^{-1} = 1e-3 \text{ s}^{-1} \end{array} \right.$$

DNA

$$\left\{ \begin{array}{l} R_T = 3.32e-11 \text{ molar} * m \\ k_{on} = 1.8e4 \text{ L}/(\text{mol-s}) \\ k_{off} = 6e-5 \text{ s}^{-1} \end{array} \right.$$

Diffusion Rates

Stokes-Einstein Equation:

$$D = \frac{k_b T}{3\pi\mu d_p}$$

Troponin & Conjugate Ab: $m = 184kDa$

$$d_p \sim (50 \times 50 \times 30)^{1/3} = 42.2 \text{ nm} \quad \longrightarrow \quad D = 4.22e-12 \text{ m}^2 / \text{s}$$

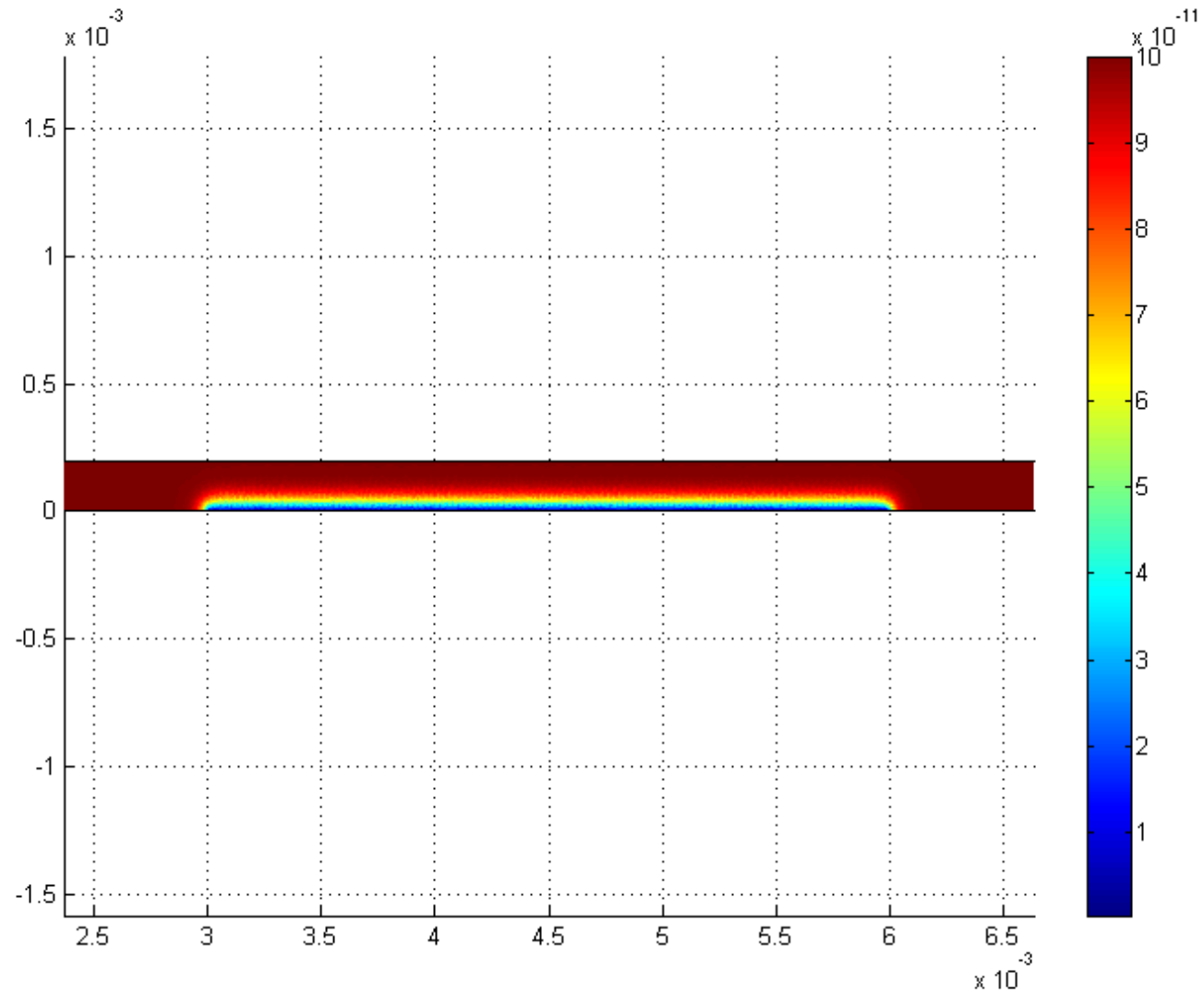
Single-stranded DNA (~200 bases)

Physical Dimension: Dia. ~0.6 nm, and a $L \sim 50$ nm

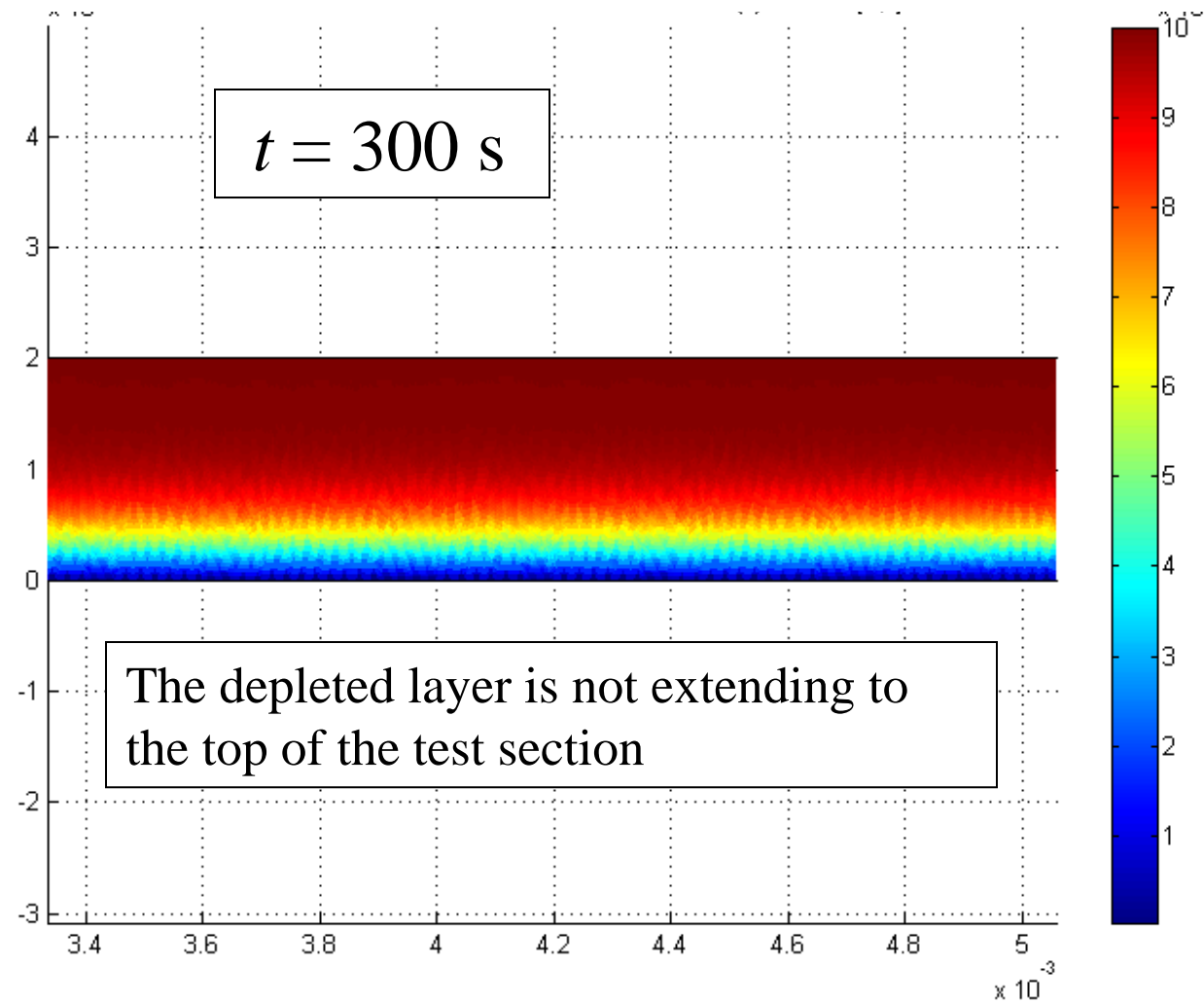
$$d_{\text{eff}} = (.6 \times .6 \times 50)^{1/3} = 2.6 \text{ nm} \quad \longrightarrow \quad D = 6.865e-11 \text{ m}^2 / \text{s}$$

Diffusion is factor ten higher for DNA

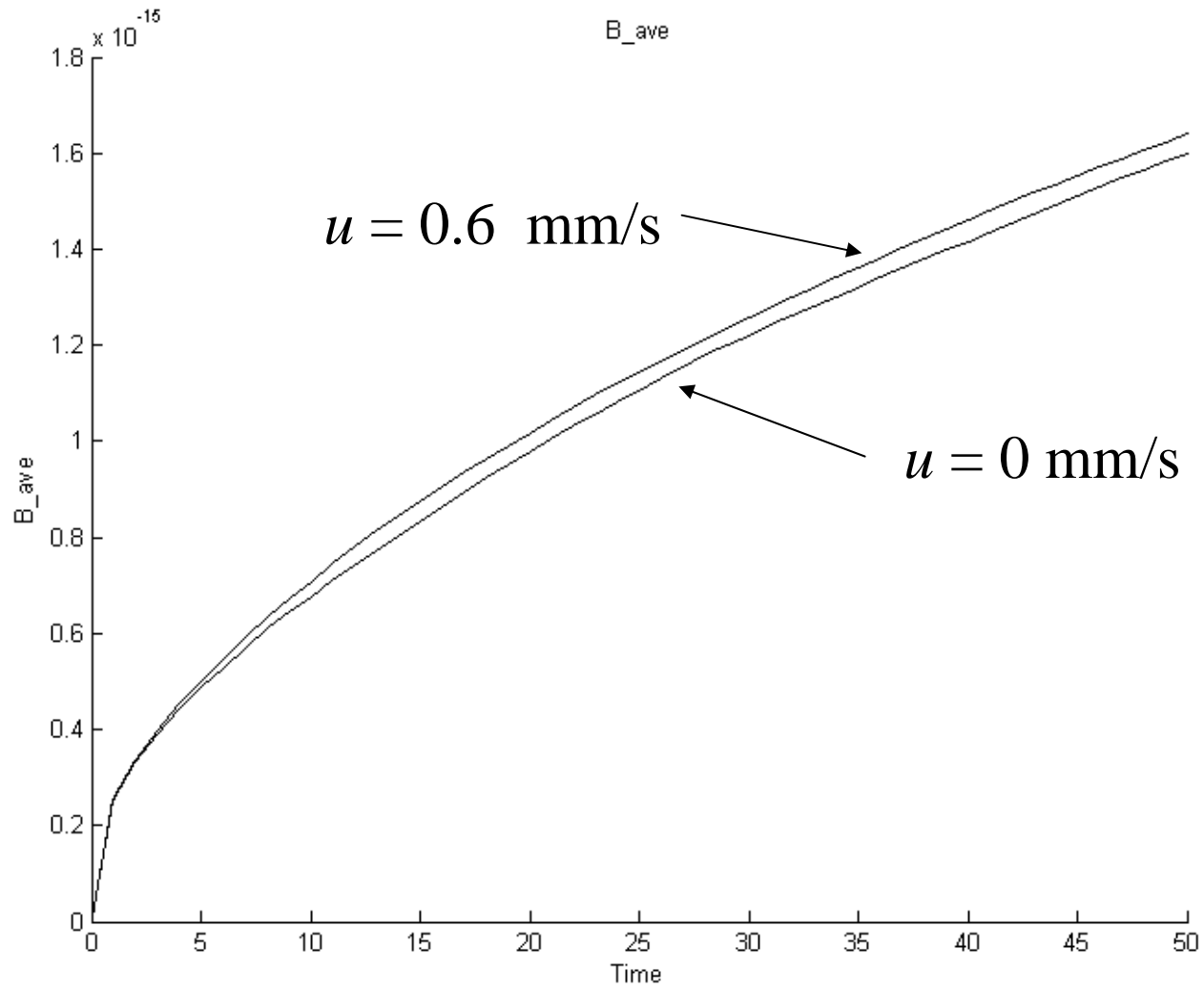
Troponin Concentration Field (t = 300 s)



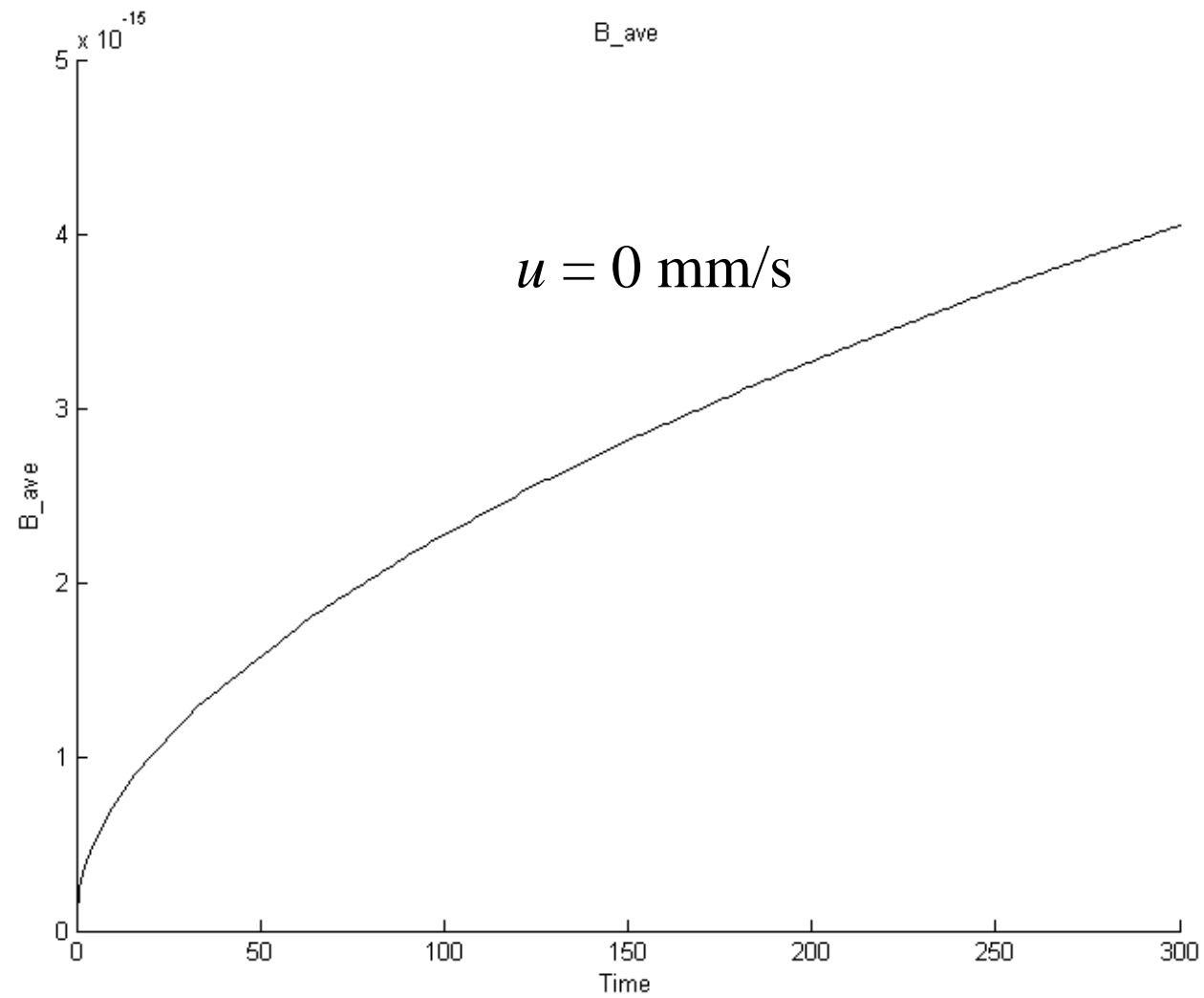
Troponin Concentration Field (Close Up)



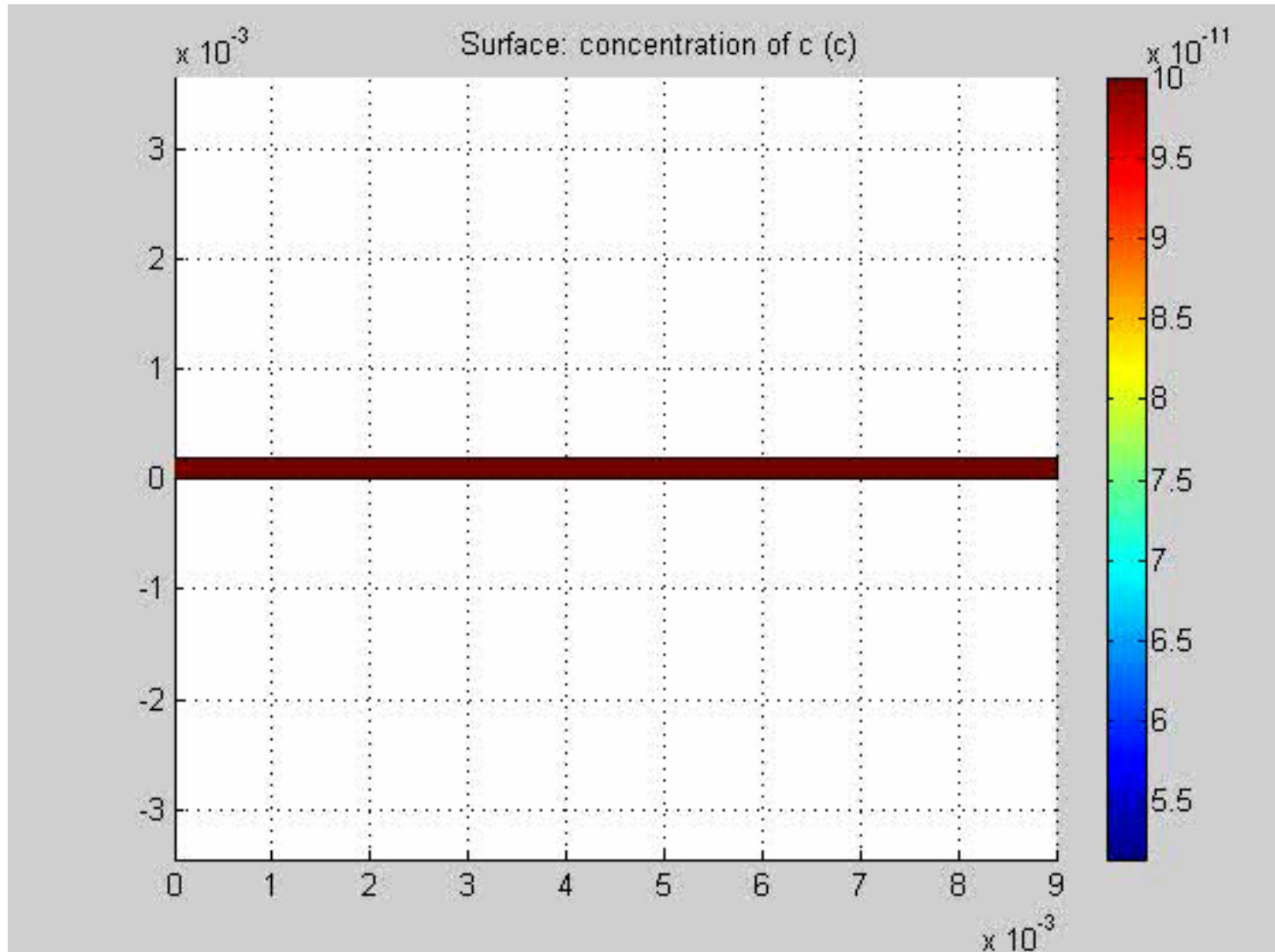
Troponin Binding Rate Curve



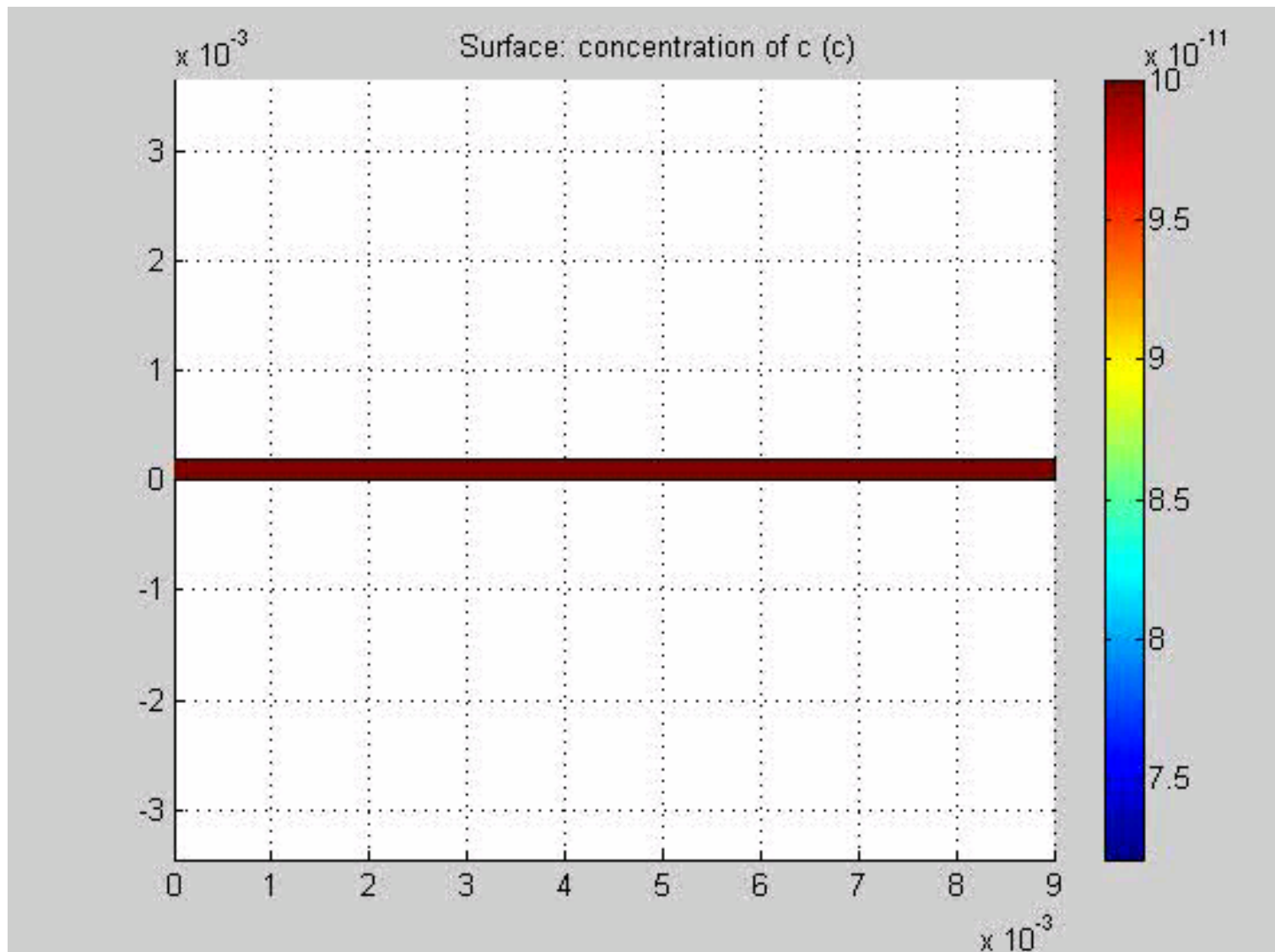
Troponin Binding Rate Curve (t=300 s)



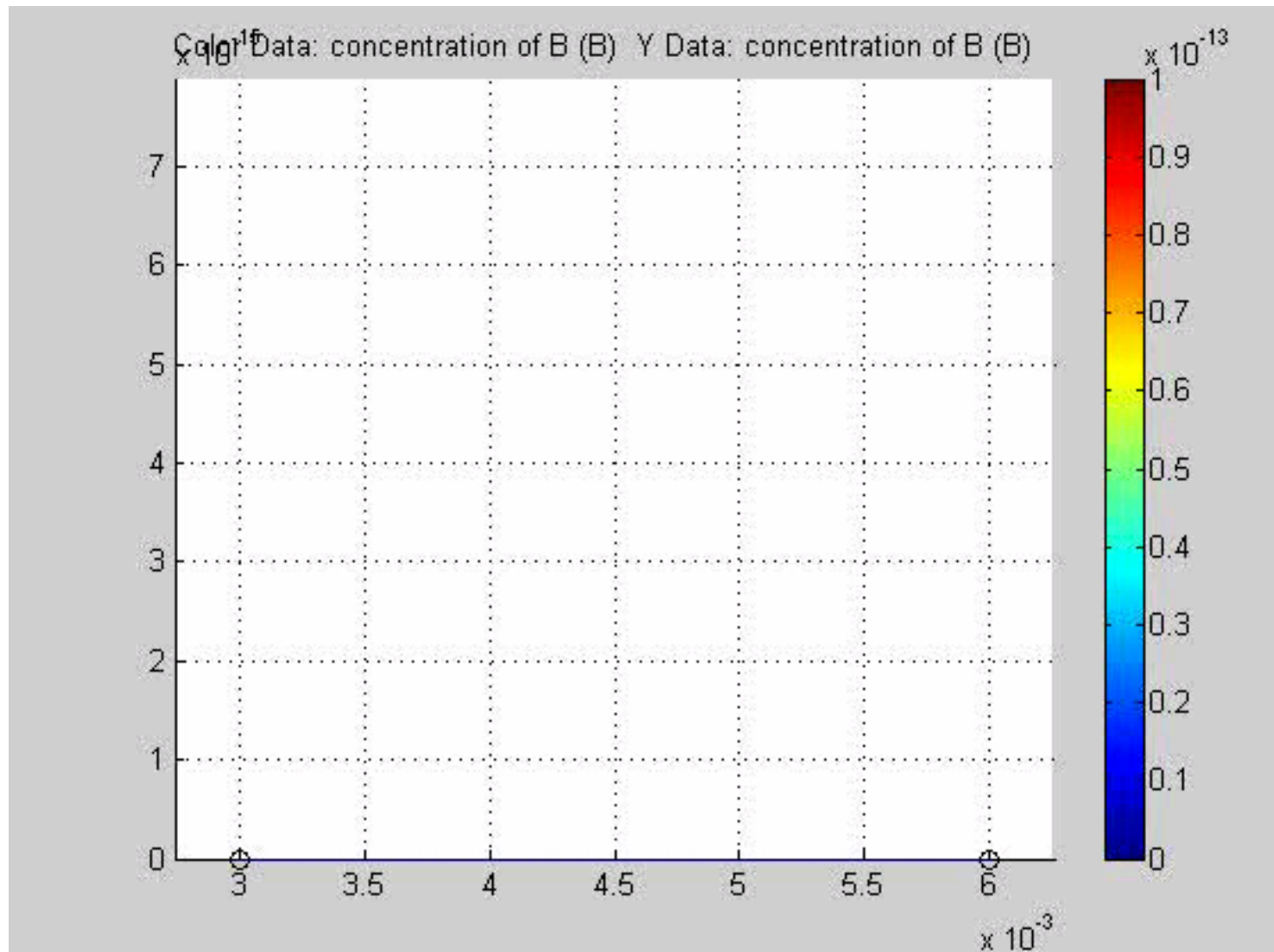
DNA Concentration Field: $u = 0$ mm/s $t = 300$ s



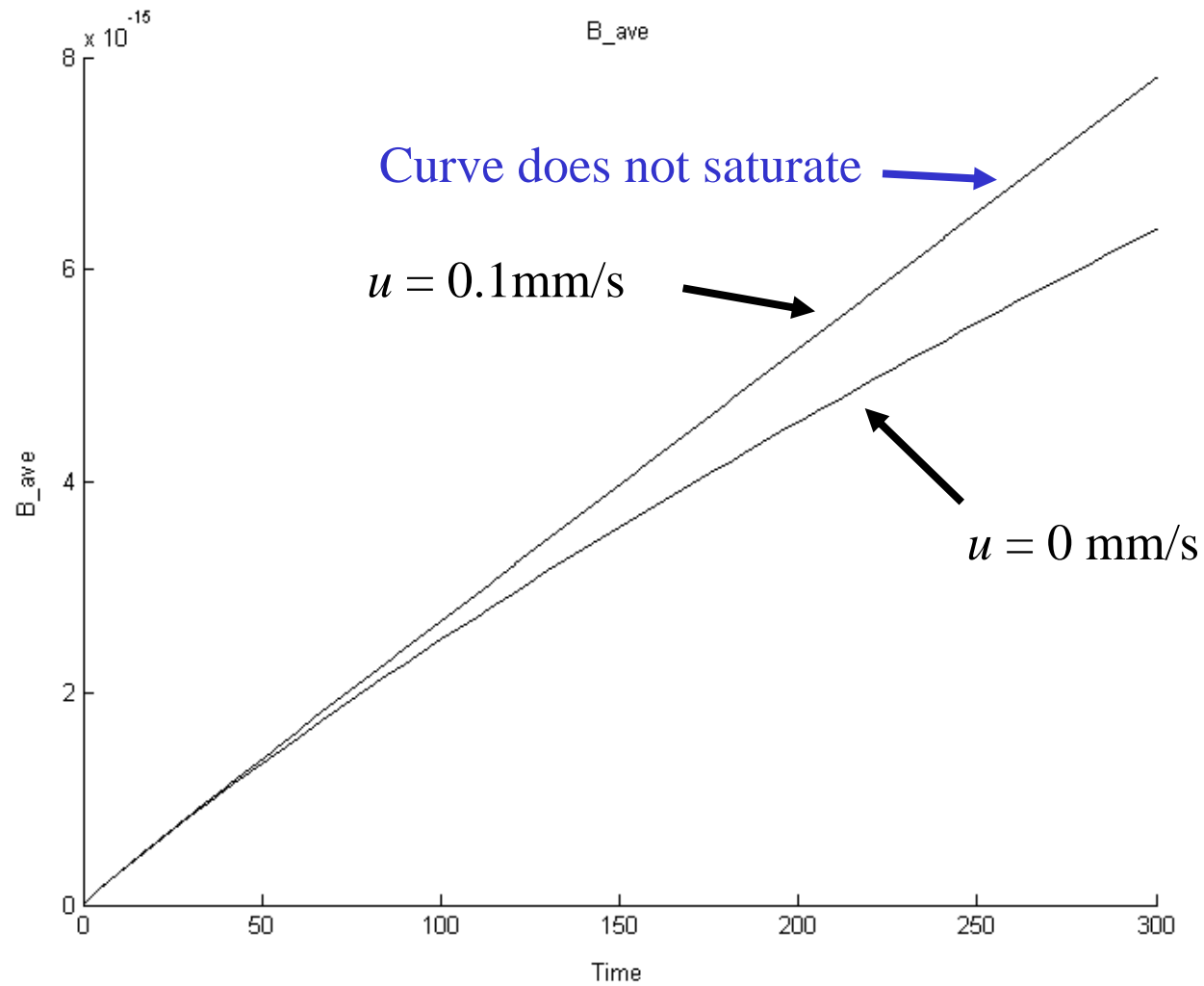
DNA Concentration Field: $u = 0.1$ mm/s, $t = 300$ s



DNA Binding Concentration ($u = 0$)



DNA Binding Rate Curve



Conclusions

- Microfluidic device is only 200 microns high
 - May limit binding for high diffusivities (i.e ssDNA)
 - Pumping fluid significantly improves binding rates for DNA (assuming has the higher diffusivity)
 - i.e. 30% after five minutes
- The easiest way to mix is to oscillate the fluid forwards and backwards using pressure
- Future devices may use electrokinetics for mixing Added complexity
 - Topic of Further Research