

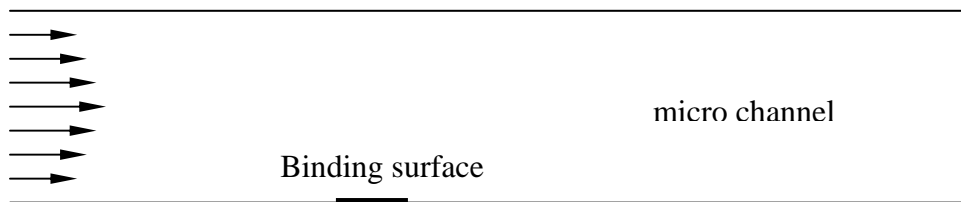
**ME141C  
INTRO TO MICROFLUIDICS**

**INSTRUCTIONS FOR HOMEWORK #2  
DIFFUSION LIMITED SURFACE REACTIONS**

**BACKGROUND**

This is an example of fluid flow in a micro channel coupled with a surface reaction taking place along the channel walls. A small concentration of a biological analyte is mixed with the fluid. The flow velocity is so small that the concentration of the analyte is transported to the reaction surface where it binds to an antibody ligand, mainly by diffusion through the fluid.

Following figure shows a rectangular micro channel. An antibody ligand is immobilized along a small portion of the top wall, called the binding surface. A binding reaction between the ligand and the analyte takes place at this surface. The analyte is introduced in the fluid at the entrance of the channel. The flow profile at the entrance of the channel is parabolic due to no-slip at the walls.



Your task is to analyze the reaction binding process between the analyte and the antibody ligand as described in the homework.

**Governing Equations**

This is a multiphysics problem and involves the following types of physics.

**1. Convection and Diffusion**

The analyte is transported to the binding surface by diffusion. The following convective scalar equation predicts the suspended concentration  $C(x, y)$  of the analyte within the micro channel.

$$\frac{\partial C}{\partial t} + \vec{u} \cdot \nabla C = D \nabla^2 C \tag{10}$$

Where,  $\vec{u}$  is the fluid velocity and  $D$  is the diffusivity of the analyte.

**Note: In this equation, isotropic diffusion was assumed. You will have to change to an anisotropic diffusion for your homework.**

**2. Reaction Binding (Diffusion)**

Following the model given by Myszka *et al.* (1998), the rate of association is  $k_{on}C_w(R_T - B)$ , where,  $k_{on}$  is the association rate constant,  $(R_T - B)$  is the available antibody ligand concentration, and  $C_w(x)$  is the suspended concentration of analyte along the wall. The rate of dissociation is  $k_{off}B$ , where,  $k_{off}$  is the dissociation rate constant, and  $B$  is the concentration of bound analyte. The time rate of change of analyte bound to the immobilized antibody is equal to the rate of association minus the rate of dissociation

$$\frac{\partial B}{\partial t} = k_{on}C_w(R_T - B) - k_{off}B \quad (11)$$

The rate of analyte binding to immobilized antibody,  $\partial B/\partial t$  must be balanced by the diffusive flux of antigen at the binding surface,  $y = 0$  such that

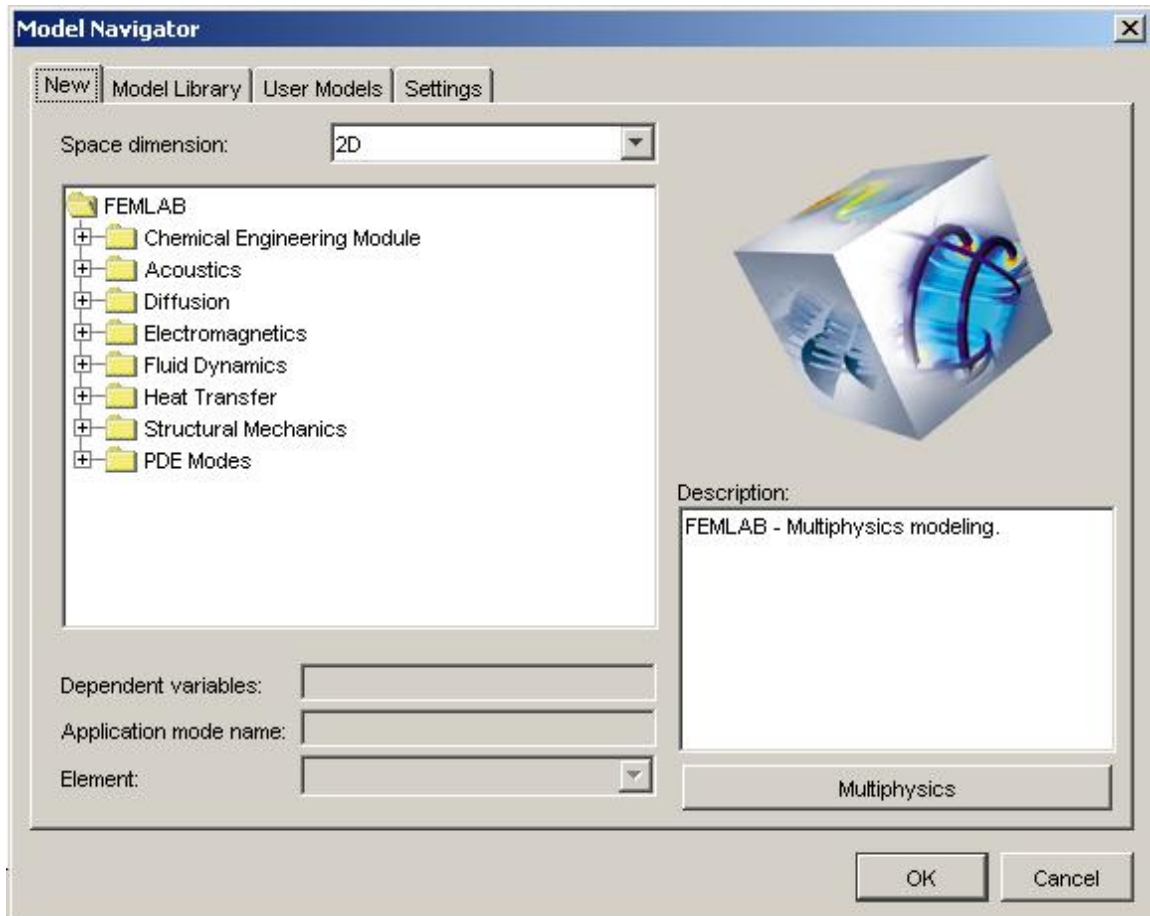
$$\frac{\partial B}{\partial t} = D \left. \frac{\partial C}{\partial y} \right|_{y=0} \quad (12)$$

Equations (10), (11) & (12) can be solved for the given immobilized antibody concentration  $R_T$  and the binding rates for different conditions can be found.

### SETTING UP THE MODEL IN FEMLAB 3.0

Femlab 3.0 is the latest version of Femlab and it can be run either with MATLAB or as a stand alone program. We will do our modeling in the stand alone program. Let's begin the modeling process.

- Click on the Femlab 3.0 icon on your desktop if you are working on Windows platform. This command starts Femlab and opens the **Model Navigator**, which looks like the following.

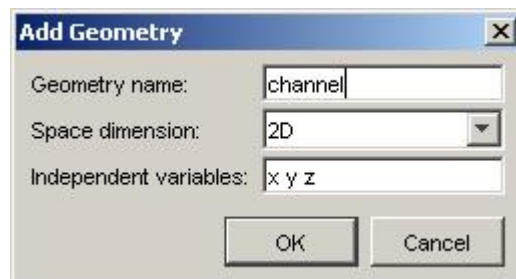


The **Model Navigator** is a multi-purpose dialog box which lets you add new geometries, and multiple physics modes in your model.

- Press the **Multiphysics** tab on the **Model Navigator**. On the subsequent page, press **Add Geometry** tab. In the subsequent dialog box, use the following settings.

**Geometry name:** channel

**Space Dimension:** 2D

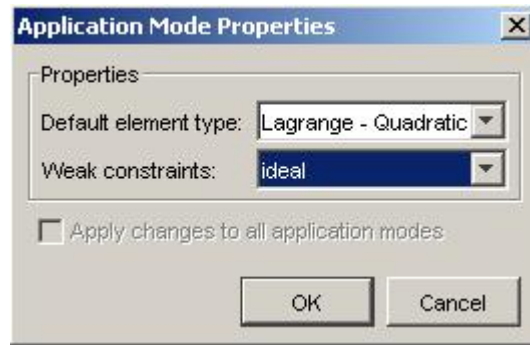


Press **OK**. It will add a 2D geometry, '**channel**' to your model. Now we will add multiple physics modes for this geometry. On the left hand side of the **Model Navigator** page, various available physics modes are shown.

Add the following modes:

**Fluid Dynamics/Incompressible Navier Stokes**

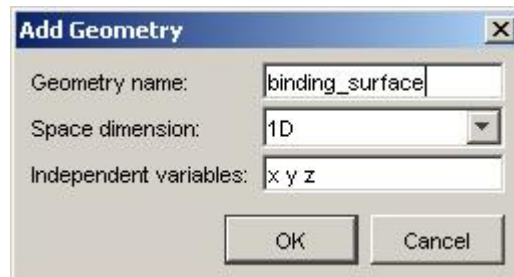
- Now we will activate the Weak constraints for this physics mode. Press the Application Mode Properties tab. In the subsequent dialog box, choose **Ideal** in the **Weak Constraint** edit field. It is important to activate the Weak constraints as we are going to solve a coupled problem using coupling variables.



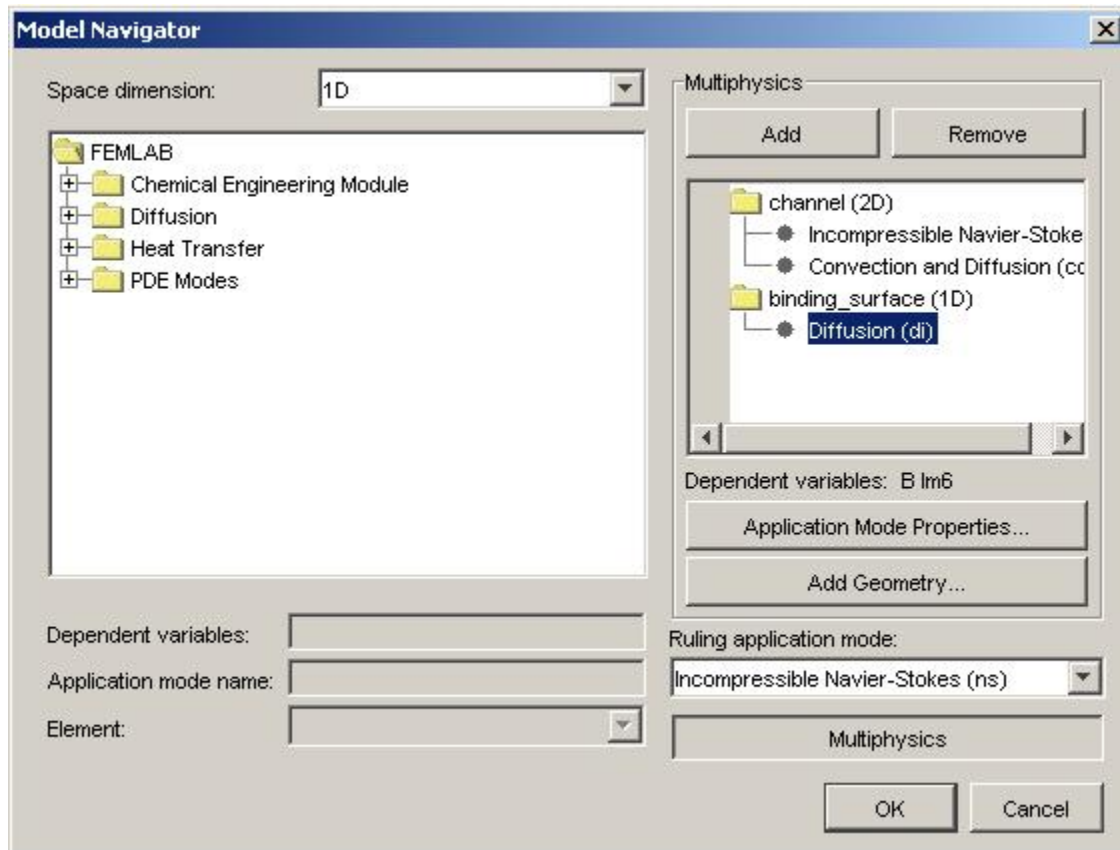
- Now add the following mode to this 2D geometry  
**Diffusion / Convection & Diffusion**
- Activate the weak constraints for this physics mode also.
- Now we will add a new 1D geometry to the model, which will serve as the binding surface. Press the **Add geometry** button. Give the following settings for the new geometry.

**Geometry name:** binding\_surface

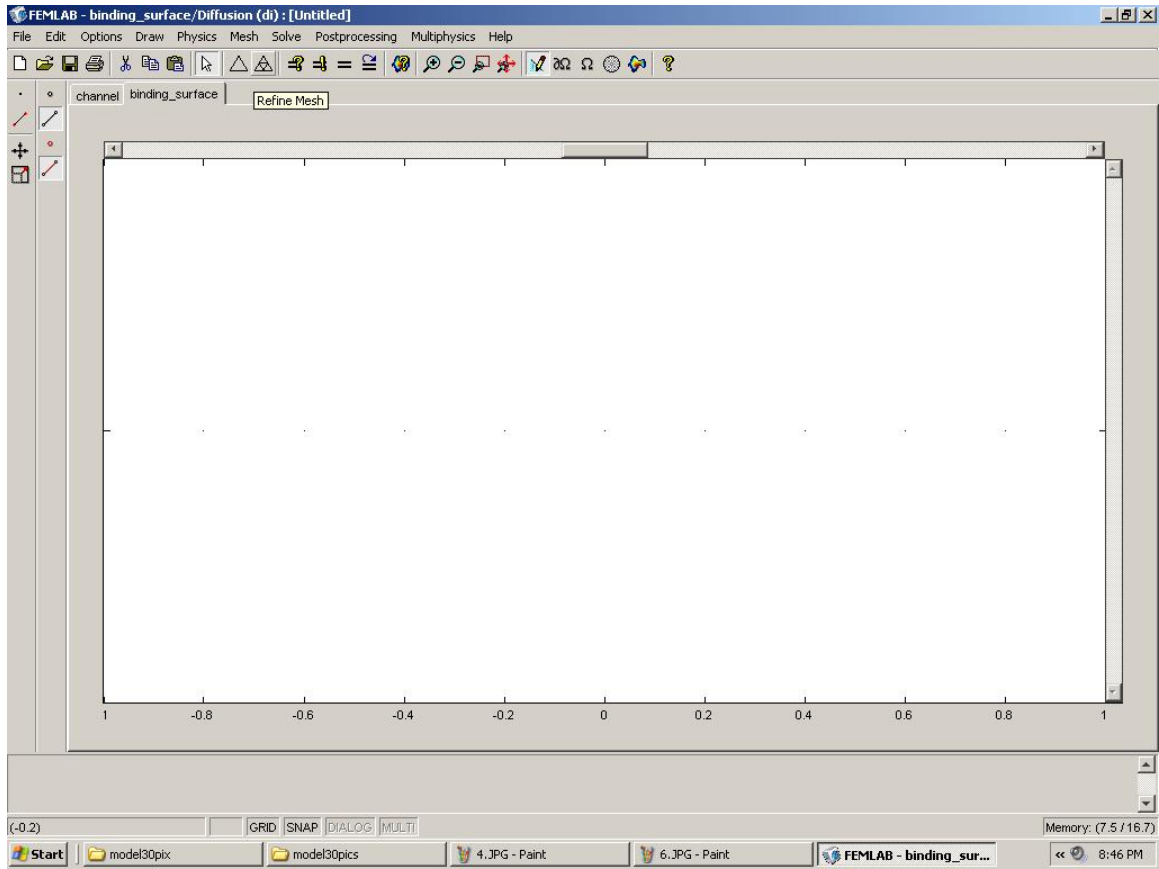
**Space Dimension:** 1D



- Press Ok to add the geometry. Select **Diffusion** physics mode from the **Diffusion** folder for this geometry. Change the **Dependent variable** name to B in the edit field on the left hand side and then press **Add**. In the following picture, one can note that the dependent variable name appears as B on the right hand side.



- Activate the weak constraints for this physics mode also.
- Now that we have finished adding geometries and physics modes, Press **OK** on the **Model Navigator** page. It will open up the FEMLAB window. On this window, you will see two tabbed pages, one for either geometry.



## ADDING CONSTANTS

We will start by adding global constants such as properties of the fluid and diffusion constants etc.

- Go to **Options** menu on the top of the Femlab window and choose **Constants...**
- In the subsequent window, add the names and the values of the constants as shown in Table 1.

**Table 1:** Constants

Name of Constant	Expression	Units	Description
u_max	1e-3	m/s	Centerline inlet velocity
c0	1e-9	M or mol/L	Inlet concentration of analyte
kon	1e8	$M^{-1}s^{-1}$	Association rate constant
koff	.02	$s^{-1}$	Dissociation rate constant
Rt	1.67e-11	Mm	Surface concentration

			of antibody ligand
Diff	1e-11	m <sup>2</sup> /s	Diffusivity of analyte
hh	.4e-4	m	Channel height (for u_para)
alpha	1	1	Size parameter

Note: In my case, the channel height is 40 micron. You will have to change to what is given in the homework.

### DRAWING 2D GEOMETRY: channel

Now we will draw the geometries. We will start with the 2D geometry, **channel**.

- Go to the **channel** page. In order to draw, one has to be in draw mode. In our case, draw mode is selected by default. However, one can go to draw mode at anytime by pressing the **Draw Mode** button on the toolbar.



The micro channel which we are going to model is of the order of few microns, while the area visible in the graphical interface is in the order of meters (SI units are default). We therefore have to change the size of the visible drawing area before we start drawing the geometry.

- Go to **Options** menu and choose **Axis/Grid properties**. In the subsequent dialog box, set the following properties on the **Axis** page.  
**x min:** -5e-5  
**x max:** 30e-05  
**y min:** 5e-05  
**y max:** 10e-05

Go to the **Grid** page. Uncheck the **Auto** radio button and set the following.

**x spacing:** 1e-5

**y spacing:** 1e-5

- Press **OK** to apply these settings. It will modify the grid axes in your FEMLAB window.
- Click on the **Rectangle/Square** button on the draw tool bar on the left in the Femlab window. Now click your left mouse button at the grid point **(0, 0)** and drag the mouse till the grid point **(2.5e-4, 0.4e-4)**—keeping the mouse button down—in order to draw a rectangle of 25e-05 by 4e-05 size.

Note: In my case, the channel length is 250 micron. You might want to change it.

- Now click the **Point** button on the draw tool bar to create points at the grid points: **(0.9e-4, 0), (1.1e-4, 0)**.

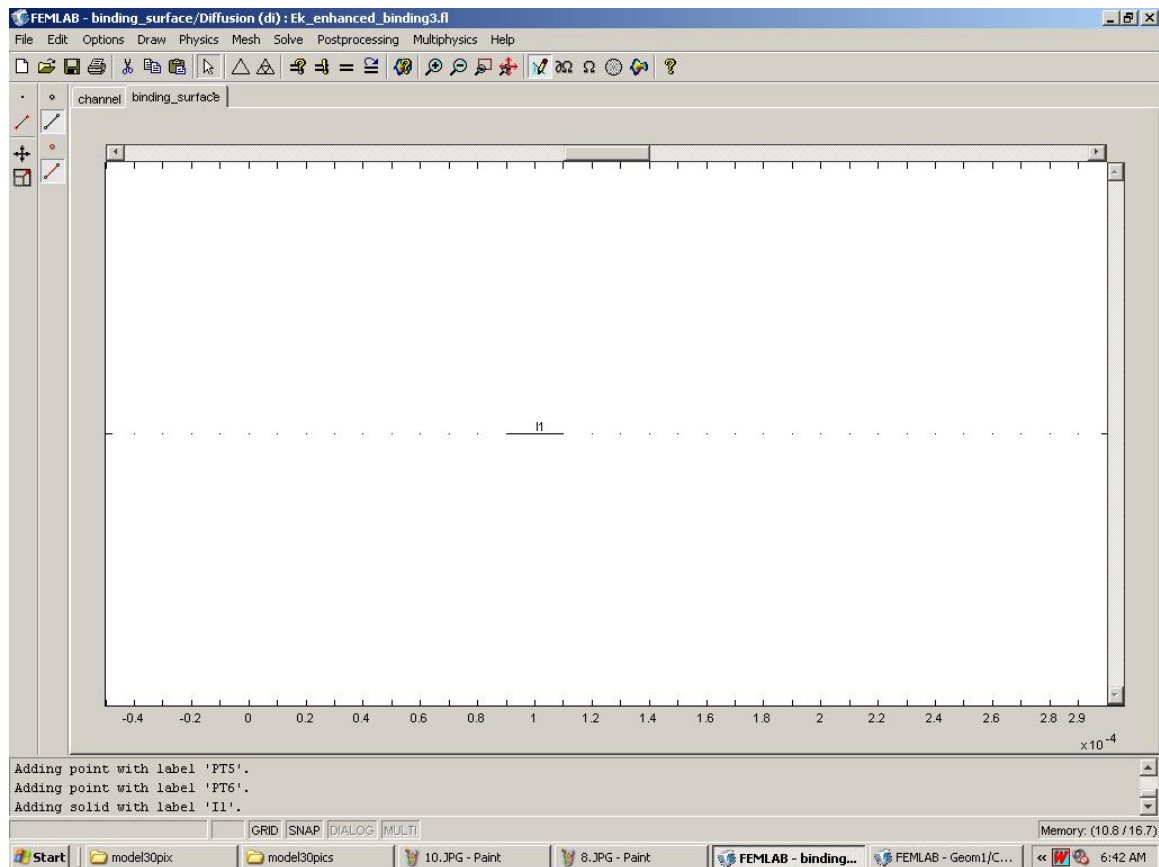
## DRAWING 1D GEOMETRY: binding\_surface

Now we will draw the 1D geometry, called **binding\_surface**. Go to the **binding\_surface** page on the FEMLAB window.

- Go to **Options** menu and choose **Axis/Grid settings**. Set the following on the **Axis** page of the dialog box.
  - x min:**  $-5e-5$
  - x max:**  $30e-05$

Set the following on the Grid page.

- x spacing:**  $1e-5$
- Now click on the **Render Edge** button on the draw tool bar and draw a line from the grid point **0.9e-4** to **1.1e-4**.



We have finished drawing the geometries. Now we will add **Expressions** and **Coupling variables**.

## ADDING EXPRESSIONS

We will need expressions for some variables like inlet velocity etc. Expressions have to be defined for the two geometries separately. First we will define them for the 2D geometry, **channel**. Go to the **channel** page in the Femlab window.

- Go to the **Options** menu on the top and choose **Expressions-> Scalar Expressions**.
- Add the following expressions in the subsequent window.

Name	Expression
u_para	$u_{max} * 4 * y / hh * (1 - y / hh)$

u\_para is the parabolic velocity profile at the entrance of the channel.

- Now we will add boundary expressions. Go to the **Options** menu and choose **Expressions-> Boundary Expressions**.
- In the subsequent window, select the binding reaction boundary (i.e. boundary no. 4) and add the following expression for this boundary.

Name	Expression
react_bulk	$k_{off} * c_{surf} - k_{on} * c * (Rt - c_{surf})$

react\_bulk is the reaction rate at the binding surface which is located at the boundary no. 5. react\_bulk will be used for specifying boundary condition in the Convection-Diffusion mode. c\_surf is a coupling variable and will be defined later.

- Now we will add expressions for the 1D geometry. Go to the **binding\_surface** page on the FEMLAB window. Go to **Options** menu and choose **Expressions-> Subdomain Expressions**. Select the subdomain 1 and add the following expression.

Name	Expression
react_surf	$k_{on} * c_{bulk} * (Rt - B) - k_{off} * B$

react\_surf is the rate of reaction for the Diffusion mode. c\_bulk is a coupling variable and will be defined later.

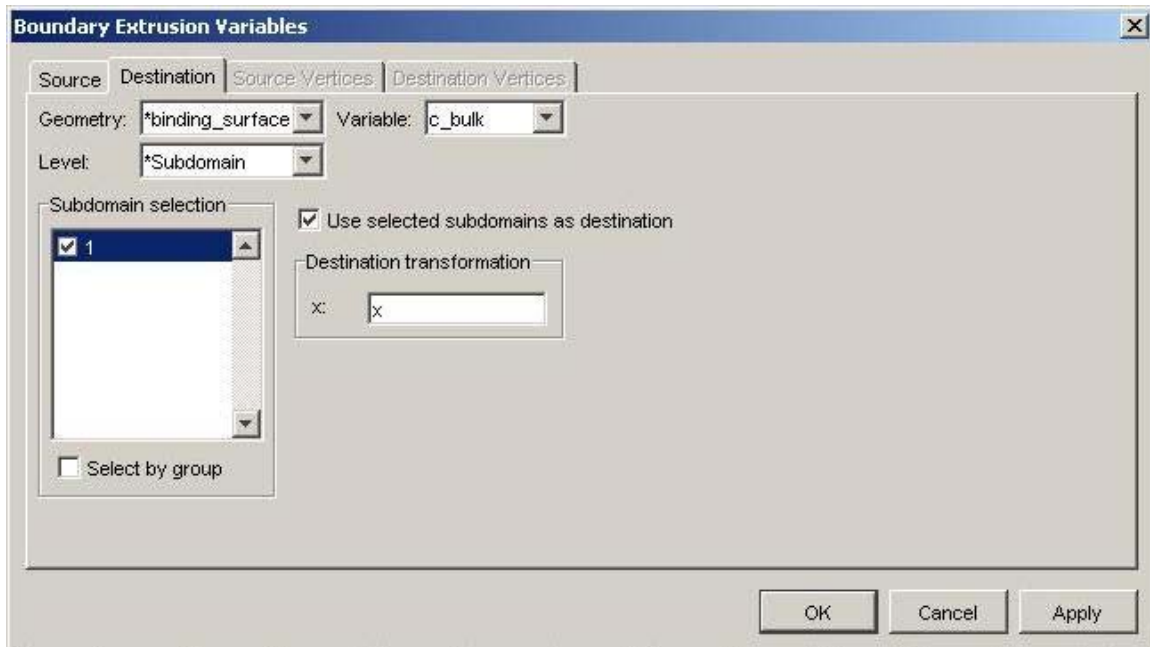
## ADDING COUPLING VARIABLES

We had noticed two coupling variables in the previous section. Coupling variables will be used for coupling the Convection-Diffusion mode and the binding surface Diffusion mode with each other.

- Go to the **channel** page. Go to **Options** menu and choose **Extrusion Coupling Variables->Boundary Variables**.
- In the subsequent dialog box, select the binding surface boundary (i.e. no. 4) and add the following expression.

Name	Expression
c_bulk	c

- On the bottom of the dialog box, select the **General Transformation** radio button.
- In the dialog box, go to the **Destination** page and select **binding\_surface** and **subdomain** in the **Geometry** and **Level** menus respectively. Check the box in front of the subdomain 1. Press **OK**.



- Now we will add the second coupling variable in the 1D geometry. Go to the **binding\_surface** page in the Femlab window. Go to **Options** menu and choose **Extrusion Coupling Variables->Subdomain Variables**.
- On the **Source** page of the dialog box, select the subdomain 1 and add the following expression.

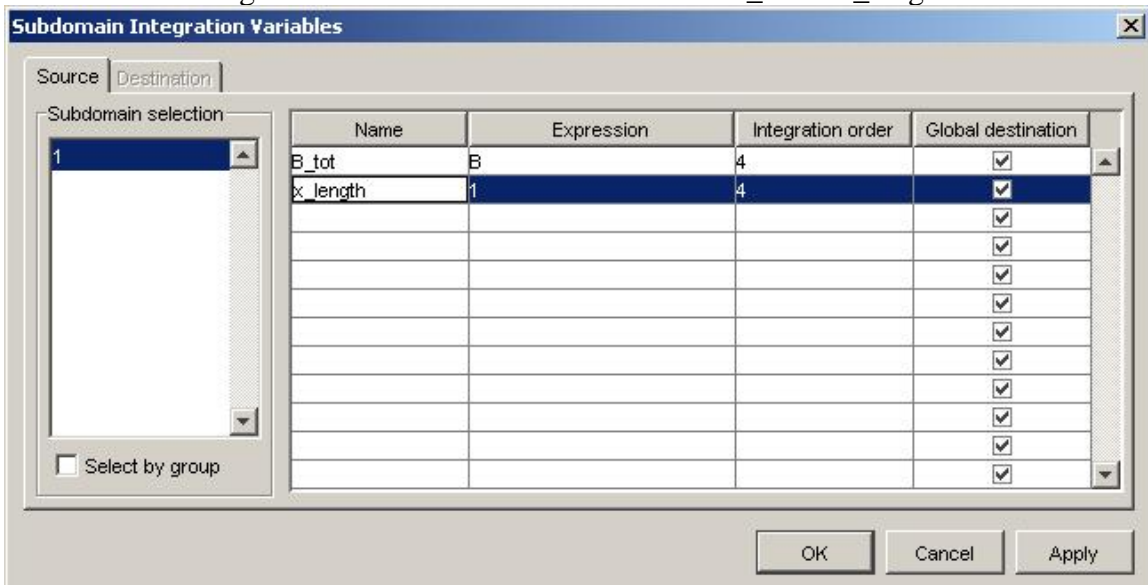
Name	Expression
c_surf	B

- On the bottom of the dialog box, select the **General Transformation** radio button.
- In the dialog box, go to the **Destination** page and select **channel** and **boundary** in the **Geometry** and **Level** menus respectively. Check the box in front of the binding surface boundary (i.e. no. 4). Press **OK**.
- Now we will add two Integration Coupling Variables for the same 1D geometry. These variables will be used for integrating the bound concentration B on the binding surface and for calculating the length of the binding surface. Go to **binding\_surface**

geometry page. Go to **Options** menu and choose **integration Coupling Variables->Subdomain Variables**. Add the following

Name	Expression	Integration Order	Global Destination
B_tot	B	4	Keep the box checked
x_length	1	4	Keep the box checked

B\_tot is the integral of B on the binding surface, x\_length is the length of the binding surface. The average bound concentration is the ratio of B\_tot to x\_length.



## SUBDOMAIN SETTINGS

Now we will start setting the coefficients and the initial conditions for the partial differential equations. This is done by defining subdomain settings for different physics modes.

### channel: Convection and Diffusion mode

- On the **Coefficients** page, select the subdomain no. 1 and set the following.
  - D isotropic = Diff (You know what you have to do here)**
  - Reaction rate = 0**
  - x-velocity = u\_para**
  - y-velocity = 0**

### binding surface: Diffusion Mode

- On the **Coefficients** page, select the subdomain no. 1 and set the following.
  - Time scaling coefficient = 1**
  - Diffusion coefficient = 0**
  - Reaction rate = react\_surf**

## BOUNDARY SETTINGS

- Now that we have defined the subdomain settings, we will proceed to define boundary conditions for all the governing partial differential equations.

### Convection and Diffusion

- Go to **Multiphysics** menu and select the **channel: Convection and Diffusion**. Go to **Physics** menu and select **Boundary settings**.
- The default boundary condition for this mode is **Insulation/Symmetry**, which is applicable for all the boundaries except inlet, binding surface and outlet boundaries.
- Select inlet boundary from the list. Select **Concentration** from the **Boundary condition** menu. Write **c0** in the **Concentration** edit field. This means that a constant concentration of the analyte is introduced at the inlet.
- Now select outlet boundary. Select **Convective flux** from the **Boundary condition** menu. This means that convection >> diffusion at the outlet.
- Now select binding surface boundary no. 4. Select **Flux** from the **Boundary condition** menu. Write **react\_bulk** in the **Inward Flux** edit field. This means that the analyte concentration is lost at this boundary due to binding reaction with the antibody. This boundary is coupled with the 1D geometry, **binding\_surface**.
- Press **OK**.

### Diffusion mode

No changes have to be made for this mode.

## MESH GENERATION

### Meshing of 2D geometry: channel

Now that we have defined all the constants, variables, subdomains settings and boundary conditions, we will move on to mesh generation for our geometries and then solve the governing equations of various physics modes. We will start by meshing 2D geometry, **channel**.

- Go to **Mesh** menu on the top of your Femlab window and select **Initialize mesh**. It will create a coarse mesh for the **channel** geometry.
- Now we will refine the mesh near the binding surface . Go to **Mesh** menu and choose **Mesh parameters**. On the dialog box, go to **Boundary** page. Select the binding surface boundary (no. 4) from the list and write **0.2e-6** in the maximum element size field.
- Press the **Remesh** button on the bottom of the dialog box. Remember that pressing **OK** will not remesh the geometry. After pressing **Remesh**, press **OK** to exit.
- Now we will mesh the 1D geometry, **binding\_surface**. Go to the **binding\_surface** page on the Femlab window. Go to the **Mesh** menu and select **Initialize mesh**. No refinement is necessary for this geometry.

## **SOLVE THE PROBLEM**

Go to **Solve** menu. Choose **Solver Parameters**. Choose the **Time Dependent** solver. Write 0:0.05:2 in the **Times** edit field.

Go to **Solve** menu. Choose **Solve Problem**.

## **POST PROCESSING**

You can make various types of plots and animations by going to **Postprocessing-> Plot parameters** and **Postprocessing-> Cross section plot parameters**. You have to do postprocessing for the two geometries separately. So go 2D geometry page and see what kind of plots you can make. Then go to the 1D geometry page and see what kind of plots you can make for this geometry. I will elaborate on this in the instruction session on Tuesday.

## **References**

[2] Myszka, D.G, 1998. Survey of the 1998 optical biosensor literature. *J Mol. Recognit.* Vol. 12, pp. 390-408.