Introduction

Transport in Adhesion Measurements. This week we will simulate convection, diffusion and adhesion of a small molecule (analyte) to a surface coated with receptor in a microfluidic channel. This simulates label-free real time assays such as SPR. We will use simple channel geometry for which the laminar flow profile is already known, so we will just simulate the transport and adhesion of the analyte. The goals this week are to learn how to build and solve a numeric model, plot results, and verify the model. First follow the tutorial to learn how to use COMSOL for this problem. Then, answer the questions in the last section of the lab, adding convection, and providing graphs and explanations as usual. *In many places, hints are added in italics that may be useful for your final project, but are not needed to build the model for this week's lab.*

Adhesion model description. You will model the amount of chemical in solution, $C(x, y, t)$, and the amount of chemical bound to the surface: $B(x, t)$. Note that one variable is defined over the entire geometry and the other only on a boundary, and has a lower dimension (1D spatial in x, vs 2D in x and y). This situation is fairly common in biological transport models, so it is useful to learn how to model this. Because there is no variation in the width of the channel, we ignore the third spatial dimension. The SPR chip has length L and height H. The bulk concentration being washed into the chamber is C_0 and the total site density of receptor on the surface is R_0. The free receptor is simply $R_0 - B$, so does not need a variable. The diffusion coefficient of C in solution is D. In this case, we assume that the bound analyte and receptors cannot move since the receptor is immobilized on a solid surface, so the diffusion coefficient of B is zero, as is its convection velocity vector. The analyte binds to the surface at rate $(R_0 - B)Ck_a$, and detaches at rate Bk_d. The complete equations for this lab are:

$$\frac{\partial C}{\partial t} = D\nabla^2 C - \nabla \cdot C\vec{V}$$

$$\frac{\partial B}{\partial t} = k_a C(R_0 - B) - k_d B$$

Recall from lecture notes about this problem that the inward flux at the reactive boundary is $-\vec{n} \cdot \vec{J} = -k_a C(R_0 - B) + k_d B$. Also recall that the fluid is pumped into the chip at a prescribed volumetric flow rate, which creates a predictable parabolic flow profile, so that fluid moves at a velocity in the x-direction of $V_x(y) = S\left[y - \frac{y^2}{H}\right]$, where S is a constant (the wall shear rate) that depends on the overall flow rate. The 8 parameters are thus $L, H, R_0, C_0, D, k_a, k_d, S$.

Tutorial: Build a COMSOL model of diffusion and surface adhesion in a closed system.

1. **Open COMSOL (classkit license) and run the model wizard**. The left panel shows the model builder menu, the central panel the Model Wizard, and the right panel the graphics. You can build a model using the Model Wizard or model builder and can add to and revise the model using the model builder. Here we will use the Wizard, but you can also right-click on the top entry in the builder menu (which is the '.mph' model file you are creating,) and select 'add model' at any time to open the wizard. In the model wizard, do the following in each menu:
    a. In 'Select Space Dimension', chose '2D' since there is no variation in concentration across the width of the channel, so it is more efficient to skip this dimension. Then click the cyan arrow to go to the next screen.
    b. In 'Add physics' chose 'chemical species transport', and 'Transport of diluted species' and click on the cyan plus sign to add it. Note that you can change the name and number of your dependent variables here, so you can rename it C to match the notation in these instructions. Then click the cyan arrow.
    c. Now click the checkered finish-line flag to exit the model wizard, and save your model somewhere you can find it later.
2. **Enter parameters:** In the model builder tab on the far left, Right-click on 'global definitions', and select 'parameters'. A window will open in the center panel for you to enter global parameters and their units. For each parameter, enter its name, and expression that includes the value and units, or an equation in terms of other values or units, or a mixture of the two. COMSOL will calculate the value in SI units. A description is optional, but a good idea, like commenting your code. Enter the values of all parameters as given below. Save your model again (and after every step).

Parameters

Name	Expression	Value	Description
H	0.02[mm]	2.0000E-5 m	channel height
L	0.6[mm]	6.0000E-4 m	channel length
D	1e-10 [m^2/s]	1.0000E-10 ...	diffusion coefficient
C0	1e-8 [mol/l]	1.0000E-5 m...	bulk concentration of anal...
R0	1e-9[mol/m^2]	1.0000E-9 m...	site density of receptor
ka	5000 [m^3/(s*mol)]	5000.0 m³/(s...	association constant
kd	0.01 [1/s]	0.010000 1/s	dissociation constant
S	100 [1/s]	100.00 1/s	wall shear rate

Note: you will change some of these temporarily while building and testing the model.

3. **Build the chamber geometry**: In the model builder tab on the far left, select Model 1

    a. In the 'model settings' tab, you can change the model identifier from 'mod1' to anything you want.

    b. In the model builder tab, select geometry. Select m for length units. You can keep the default repair tolerance.

    c. As long as the geometry tab is open, you will see a set of tool buttons above it. If you hover over these, you get text saying what they do. Or you can right click to get the list. The choices depend on the space dimensions you chose in the model wizard. If you chose 2d, you can now choose 'rectangle' and 'Rectangle1' should be added to the model builder tab under geometry; select it. In the central menu, set the dimensions as width L and height H. Position the rectangle at (0,0), with rotation angle 0. The changes you made won't show up yet, so right click on 'Form Union' and select 'Build Selected.' You may need to rescale your window by pressing the "Zoom extents" symbol  in the menu at the top of the graphics window. Now you should see your rectangle with correct dimensions. Save your model. *Note: if at any time you have trouble seeing or solving your model because of the long thin geometry, you may want to temporarily set L = 3*H, but remember to set it back by the end.*

    d. *For more information, a great tutorial for defining more complex geometries is at: http://www.comsol.com/products/tutorials/introduction/page8/. Also, you can load the geometry from a file created by other 3D drawing programs.*

4. **Enter Equations**. In the model builder tab,

    a. Expand the 'Transport of diluted species' section by clicking on the tiny plus sign, and click on 'Convection and Diffusion'. Expand the 'Equation' section by clicking on the tiny triangle, to compare the equation to the ones you learned in class so you know how your parameters relate to the coefficients in the equation. (COMSOL uses Nj instead of J for flux)

    b. **Adjust equation parameters**. Expand the sections to see where to enter the diffusion coefficient, which is your parameter D, and the velocity field from the equations $V_x(x,y) = S\left[y - \frac{y^2}{H}\right]$, and $V_y(x,y) = 0$.

    c. **Set initial conditions**. Click on 'initial values', and enter 0, so the chamber starts empty. *Hints for independent work: if you want to have initial values that depend on position, this can simply be defined by using a function of the spatial variables here.*

    d. **Set boundary conditions and boundary reactions**.

        i. Note that there is already a 'No Flux 1' condition set, which is applied by default to all four boundaries, so the default is a closed system.

ii. You want the top of the chip to be closed, but the left boundary will be 'inflow' at concentration C0, the right 'outflow', and the bottom will have adsorption as the boundary condition. Right-click on 'Transport of Diluted Species', and select inflow from the list of boundary conditions, remembering to set the parameter in the central panel. To apply this condition to the left boundary, click on this boundary in the graphics window, then click on the cyan plus sign in the Boundary Selection central panel. Now any time you click on 'inflow' you should see those boundaries highlighted in blue.

iii. Do similar steps for outflow on the right boundary. Note that any boundaries you add are automatically removed from the 'No Flux 1' condition, since it is set to be overridden.

iv. Now, you need to add the absorbing lower boundary, which will be modeled as a flux since C leaves as it turns into B. Right-click on the 'Transport of Diluted Species', and select 'Flux' from the list of boundary conditions. Apply this to your lower boundary and click on species C to indicate that this condition applies to species C at the lower boundary. Then expand 'Inward Flux' and select the species C box, so it applies to your variable C. This will open a place for you to enter the reaction equation that defines the *inward flux*: that is the increase in C at the surface, at this boundary: kd*B - ka*C*(R0-B). This will be highlighted to indicate an error. In general, you see this if you use an undefined variable or if the units are not correct for your expression. Always solve the problem when text is highlighted in color by COMSOL. In this case, we need to define B.

5. **Add boundary variable B and its equations.** Since you want to model the dependent variable B on this boundary, we need to add more physics, this time in the 1D surface.

   a. Right click on "Model " and select 'Add physics' then expand Mathematics → PDE interfaces → Lower dimensions → General form boundary PDE and click on the plus sign below that section to add this to the physics of the model. On the central menu that opens, rename the one variable B, and press the finish line flag. Now you can adjust this part of the model by selecting 'General Form Boundary PDE (gb) on the Model Builder menu. Under Boundary Selection, set this to only apply to your lower boundary. Under Units, set the units of the dependent variable to be in surface site concentration (mol/m^2) and the units in the source term quantity to be molar flux (mol/(m^2*s)).

   b. Now click on the 'General form PDE 1' submenu, to enter the reaction equations in the source term. In this boundary, the complex can't move along the surface, so the diffusion coefficient and convection variables are all zero. However, there is a reaction, which is the negative of the reaction you entered previously. Look

at the form of the equation to make sure you are entering the correct values in all the parameters so that your equation will be simply $\frac{\partial B}{\partial t} = k_a C(R_0 - B) - k_d B$.

c. Make sure the initial value for B is 0, since there is no complex at the start.

d. Now return to the boundary condition that you defined using B and make sure it no longer appears as an error.

6. **Mesh the model**: under the model in the model builder tab, select mesh. The default is 'physics controlled mesh' in which the mesh is determined dynamically, which is a good default.

   a. **Make the mesh**. Right click on it, and select 'Build Selected', and your mesh should appear in the graphics window.

   b. **If you want to change the mesh size**. Under mesh settings, try a more fine or more course mesh. Then select 'build all' above the central window, or 'build all' after rightclicking on 'mesh 1' or 'build selected' under 'Mapped 1'. Since you only have one geometry region, build selected and build all give the same result; if you have multiple regions, you can rebuild the mesh for just the selected region or the whole model. (You can also right-click on 'Mesh 1' and add a 'Size' object, which allows you to just change the size of this mesh, in which case it overrides the size under 'Mesh 1'. Again, if you had multiple regions, you might select different mesh sizes on each one.

   c. **If you want to change the mesh type**. To change the type of mesh, disable or delete the existing mesh, and right click on 'Mesh 1' to get a list of mesh types you can add, and then repeat the process above. Try out different meshes to see how they look. All meshes have properties you can change in addition to the size. Because your solution will change sharply near the inflow and absorption boundaries, we recommend you try the 'Boundary Layers' mesh, and identify these boundaries to be treated, or select a mesh the adapts to the physics of the problem.

7. **Solve the model**: at the very top of the model builder, under the file name *(root)*, right click to select 'Add Study'.

   a. Under preset studies, chose 'Time Dependent' and press finish. You should see the study 1 show up in the Model Builder tab. Click on study1, and select compute by clicking on the equals sign in the toolbar or in the right-click menu. You should see the model solve in real time in the default display in the graphics window. If it doesn't show in real time, click on "Study 1" and 'Time Dependent 1' and expand 'Results while Solving' to make sure that the 'plot' box is checked, then run again.

   b. **Change the temporal range and resolution of the output if needed**. Click on 'Time Dependent 1' to change the 'Times' of the simulation, in the format:

range(start,stepsize,end). Use this to adjust the duration of the simulation and the values at which output is saved. However, COMSOL takes whatever integration step sizes it needs to match your tolerance requirements, and then interpolates between integration time steps to get your output times, so you can't use this range of times to affect the accuracy of your simulations. Instead, you need to adjust the tolerance. COMSOL has both a Relative Tolerance (RTol), and also an Absolute Tolerance (ATol), and it uses the LESS stringent of the two to determine the integration step size while time stepping. That is, it checks whether the error created in the step is less than RTol*y+ATol, where y is the current system state. As noted online http://www.comsol.com/community/forums/general/thread/13859: "This means that the absolute tolerance almost always has to be modified since there is no way of giving a good general default value. As a first approach, it may be a good idea to use a very small absolute tolerance. This makes the relative tolerance the ruling criterion for the error control." Another option is to set the absolute tolerance as 0.1% of the expected size of your variable values (e.g. 0.001*C0). To change the Relative Tolerance, look near the top of the Time Dependent settings. To change the Absolute Tolerance, see the 'Solver Configurations' → 'Solver X' → 'Time Dependent Solver X'. You will almost certainly need this today, since C has such small absolute values.

c. **Change the spatial resolution**. Use a finer or different mesh and see if it affects the appearance of the simulation during solving. Chose a mesh that is efficient but does not cause obvious artifacts. (Now that you've seen the solution, you can see what regions of the geometry have high spatial gradients; these need finer mesh sizes, but the simulation will run faster if you don't use a fine mesh over the entire geometry, so consider using meshing methods such as 'corner refinement' and 'boundary layers' to make simulations both accurate and efficient, if the defaults are not working for you.)

d. **How to decide if you need to improve the temporal resolution**: To determine this, you will need to view how a variable changes over time, which we do in section 8 below. If you are not concerned with the time dependent solution, and only interested in steady state, then this does not matter.

8. **Plot results**. Here we will learn how to view results in COMSOL. You may want to return to this section when you need to make plots for problem 1 in the lab.

a. **Default surface plots**. You have already noticed that you can see the value of your dependent variable C on the surface over time during the simulation, and that you can see the final values at the end of the simulation. As long as the "generate default plots' box is checked in the central 'study settings' window when you select 'Study 1,' the simulation will produce plots of all your dependent variables. You can find all your plots under 'Results'. To see your variable C, click on 'Concentration', and this will open a 2D Plot Group in the

central window, where you can change the time to view the solution at any time of interest. (Click 'Plot' at the top of the central window to apply your change, and see the graphics window change). To see your variable B, click on '2D Plot Group 2' under 'Results', and you will see that just the bottom line is colored. open up the submenu by clicking the '+' sign, and click on 'Line 1' and you will see that the variable being plotted is B.

i. **autoscaling**: One thing you might notice is that the color bar legend is always changing, since the system is autoscaling. It is often helpful to see the system run with a consistent scale that you set manually. To do this, select 'Results' and find the figure with your 2D color plot showing concentration, which should have appeared automatically, and expand the item in the Model Builder Menu so you can click on the "surface 1" plot. Check the box for 'Manual color range' and set the minimum to 0, or any other value that you calculate as relevant. (Note: for some reason, you can't use parameter values to set the min and max in the ranges of figures.)

b. **Line Plots**. Create your own plot of a line as it changes over time. For example, we might want to plot the concentration of C in the chamber near the surface, since this is what is available to bind (y = 0). We can plot C(x,0) at several time points to accomplish this. Or, we might want to plot C(L/2,y) to see how the concentration changes with height half-way down the channel.

i. The first step is to define your line. Right click on 'Results' submenu 'Data Sets' and select 'Cut Line 2D' because you want a line from a 2D variable, C. Once you add a new Cut Line 2D, you can rename it something informative like 'chamber height cut line'. Use the central window to define your cut line. For example, the default is two points, so you can use the points (L/2,0) to (L/2,H). Click 'Plot' at the top, and you should see your red line appear in the graphics window so you can make sure you got what you wanted.

ii. To make a graph using this line, right click on 'results' and add a new 1D plot group, then right click on this and add a 'line graph'. This is like opening a figure and then adding a line to the figure. It is two separate steps since it allows you to add more than one line to the same figure. In either the '1D Plot Group 1' or the 'Line Graph 1', use the central window to indicate that the data set is that line you just cut (eg chamber height cut line). Alternatively, try plotting C(x,0) by selecting 'Solution 1' as the 'Data set', and then manually selecting the lower boundary in the 'Selection' section. (You can change the Data set in either the Line Graph, or the parent Plot Group; it doesn't matter if you only are plotting one Line Graph.) In the central window, you can also indicate which time points you want to plot using 'Time selection'. Enter 'all' or select one or

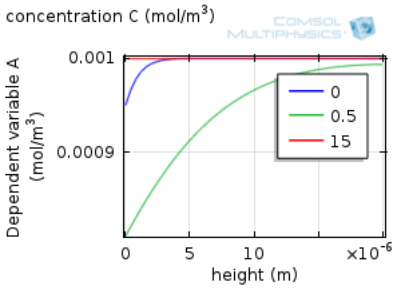
more time points from the list. Make sure the y-axis data expression is 'C', so it plots your solution concentration. The default is arc length, which works fine here since the 'arc' is the line you defined that went from x = 0 to x = L, so the arc-length is the same as the x-coordinate. However, you can explicitly assign the x-axis to 'expression' which you then define as 'x', with units 'm' and call it 'position in channel'. You are ready, so click on 'plot' at the top of the central panel, and your plot should appear in the graphics window. Also click on 'show legend' so you can see which time points you are graphing.

c. **Plot a single point over time**. As an example, we may want to plot the amount of bound species at the center of the lower chamber wall: B(L/2, 0). This time, define a cut point 2D (since your simulation is still a 2D system), and enter the coordinate. Check the box that says 'snap to closest boundary' to guarantee that this point is on the boundary, since B is only defined on the boundary, so numerically close to the boundary is not good enough. Now press 'plot' to see your point as a red dot. Now add a new '1D Plot Group', and add a 'Point Graph' to it. Chose 'bottom center' as the data set, and 'B' as the y-axis data expression, and use 'time' as the x-axis data parameter. Then choose plot. You should see how B changes over time.

d. *Additional comments for independent projects: See also the "Results" section that covers how to build plots, in http://www.comsol.com/products/tutorials/introduction/page2/ most of the way down the page. Their notes are particularly helpful for 3D models, which require re-orienting the surface at times.*

9. **Exporting plots**. There are several ways to export data from COMSOL.

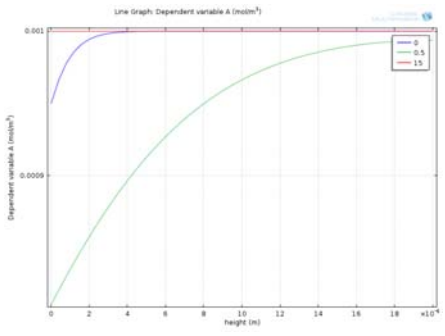
a. Note that COMSOL autoscales line plots by default as well as surface plots. Both can be misleading since the plot will show what appears to be a large change until you notice by the scale that the change is actually insignificant. To avoid exporting a misleading graph, pay attention to the axis that corresponds to the dependent variable value, and if it does not start at 0, decide if you are trying to emphasize small differences, or if you want to manually scale to include the zero value. Do this by setting the range in a surface plot, the axis in a line plot, etc. Note that the range is controlled on the surface group, while the axis, which must be common to all lines that are included on one plot, is controlled on the plot group.



b. **Add a plot to your export category** by right-clicking on the plot and selecting "add image to export". Then find the object in the Export category under Results, select it, and modify the central panel to determine the export. Note that you can adjust the size of the image, which is different than shrinking it after saving the file (see comparison to the right). Make sure you give it a filename and select 'include' under layout to get the labels and titles in your graph. Then click 'export' at the top of the central panel. This will overwrite another file with the same name without asking you, so if you want to save multiple version of the same plot, you need to change the file name.

c. You can also export data files that you can then open in Excel to plot, or in MATLAB or other such programs to perform additional calculations. We will do this next week.

d. COMSOL can be used with MATLAB to do complex tasks like parameter estimation. Also, a LiveLink™ interface for Matlab® is available for those who want to incorporate a COMSOL Multiphysics model into an extended programming environment.



Lab 4 Assignment:

1. **(15 points) Verify your model stepwise**.
    a. (5 points) What are the equilibrium values of B(x) and C(x,y) that obtain, and are these what you would expect? Explain.
    b. (3 points) What are characteristic times that may govern this simulation, and how do these compare to the time scale you needed to reach equilibrium? Support your answer with a plot of B(L/2) versus time. (*Hint: to get numeric values of your characteristic times, you can define them according to their formulas in the parameters window, and COMSOL will calculate their values for you.*)
    c. (2 points) Show a color 2D plot of the solution C(x,y) at a characteristic time you think is important; that is, show a plot in the middle of the transient phase of the simulation. Does the pattern make sense?
    d. (5 points) Describe ways to modify the model to verify separately that adorption and desorption, convection, and diffusion are each working correctly? That is, how might you test just adsorption, just convection, and just diffusion, and what would you expect to see? If you have concerns about any of these in your model, perform these tests and either confirm or fix each of these components, but you don't need to show your results.
2. **(10 points) Use your model to simulate a realistic BiaCore SPR experiment** with 2 modifications. (1) Your SPR experiment starts with no chemical in the channel, then you inject the chemical at a concentration C0 for 100 seconds, then wash it out for another 200 seconds. *Hint: To create a time-dependent inflow, use the variable 't' in the equation for concentration in the inflow. For example, you could use C0*t/[100 s], which would increase the inflow concentration linearly at a rate of C0 per 100 seconds. More to the point here, you can use an expression similar to 'if(t>2[s],1,0)', which takes the value of 0 for t < 2s and 1 for t > 2s. You can always use equations, but you need to be rigorous about units, so the if-example here needs modification so the result is in concentration units. If you get solving errors at the time of this sudden change, you will need to change something about the tolerances or the solving algorithm, just as we learned in MATLAB. e.g try deselecting relative tolerance. Another option is to force the solver to end a time step at the exact time when the injection switches. You can do this by including this time in the list of output times, and selecting 'strict' under 'Time stepping' in the central window that opens when you click on: Study 1 → Solver configurations → Solver 1 → Time dependent solver* (2) An SPR device records the average response over the entire lower surface of the chip. *Hint: Right-click on 'Results → Derived Values' to open a menu, from which you can select operations like integration, average, maximum, etc. The derived values are used to make table, which appears below the graphics window. You can plot the data in a table by pressing the buttons above the data table, or by moving back to an existing Plot Group and adding a 'Table Graph'.*
    a. (10 points) Plot $B(x,t)$ averaged over all x along with $B(0,t)$, $B(L/2,t)$ and $B(L,t)$ all together on the same plot and interpret/explain the results.

Some hints that helped make the model more robust or faster in previous years:

1) *Set your output times so that one of them is the switch time, and use intermediate time stepping, which forces the simulation to use output times plus any additional times. This prevents the simulation from trying to jump past the switch in the middle of a time step.*
2) *use 'generalized alpha' instead of 'BDF' as the method in timestepping.*
3) *Deselect relative tolerance, and use an absolute tolerance that is 0.1% of the maximum value (eg C0), so you don't move too slowly when the concentration suddenly changes at the start and switch.*
4) *use a boundary mesh that enhances meshes only on the boundary(s) where change is important.*

3. **(10 points) Model multiple concentrations in an SPR experiment**. SPR experiments are performed using several values of C_0 in separate injections. Between each wash step and the next injection, the chip is 'regenerated' to remove all the bound analyte and restore the receptor. The results are plotted in parallel on a single graph (see figure 6A in this week's paper). Model a typical SPR experiment, using the parameters from lab 4 ($H = 0.02\ mm, L = 0.6\ mm, D = 10^{-10}\frac{m^2}{s}, R_0 = \frac{10^{-9} mol}{m^2}$, $k_a = 5000\frac{m^3}{mol\ s}, k_d = 0.01\frac{1}{s}, S = 100\frac{1}{s}$), and alter C_0 to result in the following values for the ratio of input concentration to dissociation constant $K_d = k_d/k_a$: $C_0/K_d = 0.1, 0.3, 1, 3, and\ 10$.
    a. (5 points) Show the response for all five runs on a single figure
    b. (3 points) Plot both B_{SS} and max(B) as a function of C_0 on a separate figure
    c. (2 points) Interpret these two plots.

   (*Hint: The simulations can be done in COMSOL using a 'parametric sweep' which runs the same simulation with multiple values of one or more parameters. Find parametric sweep by right-clicking on the 'study'. Press the plus sign and Select the parameter to be changed from the drop-down list. Since you are plotting 5 simulations on one graph, you just want one curve per simulation. What is the measurement that best represents response?)*

4. **(5 points) Compare the PDE to two ODE models**. The **rapid mixing** model assumes $C = C_0$ even near the surface. This is modeled by the ODE:

$$\frac{dB}{dt} = k_a C_0 (R_0 - B) - k_d B$$

   The **two compartment** model assumes two compartments: one compartment stays at the inflow concentration C_0, while the other is the near-surface compartment, and is represented by the variable C. Material moves between these with a permeability k_M (in m/s). We use S to indicate flow rate, while Myska et al use the maximum velocity, which is in the center of the channel: $v_c = V\left(\frac{H}{2}\right) = \frac{SH}{4}$, so our form of the equation is a bit different than that of Myszka et al. We use: $k_M \sim 1.282\left(\frac{SD^2}{4L}\right)^{1/3}$. The two-compartment ODE is then:

$$\frac{dC}{dt} = \frac{1}{h_i}\left(-k_a C(R_0 - B) + k_d B + k_M(C_0 - C)\right)$$

$$\frac{dB}{dt} = k_a C(R_0 - B) - k_d B$$

Where h_i is the height of the boundary layer. If we make a quasi steady state assumption that C is responding instantly to changes in B, then we can set $\frac{dC}{dt} = 0$ to solve for C, which we can then replace into the equation for $\frac{dB}{dt}$. This eliminates the dependence of height of the boundary layer, and produces an ODE in one variable, which we still call the two-compartment model:

$$\frac{dB}{dt} = \frac{k_a k_M C_0(R_0 - B) - k_d k_M B}{k_a(R_0 - B) + k_M}$$

a. (4 points) Using your simulations from question 1, compare the PDE model to these two ODE models. *Hint: compare the three models in a single graph. One way to do this is to export the PDE model results to a table you can open in MATLAB.*
b. (1 point) Which is the best of the 3 models for this set of parameters? *Hint: discuss the graph. The best model is the simplest accurate model.*