Homework 7

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BIOENG 104 Biological Transport Phenomena | Aaron Streets

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1 Problem 1

Complete the Google survey here by Friday, March 8th, 11:00 am.
https://forms.gle/p99evawh8GWchfg6A

Completed!

2 Problem 2

Find a peer reviewed manuscript that uses COMSOL or another numerical simulation to model transport by diffusion or flow to analyze a biomedical device or biological system. Summarize the study in one to two paragraphs. Make sure to state the goal of the study and the major findings. Provide a citation for the study in NLM format.

In a paper published in *Biomechanics and Modeling in Mechanobiology* in 2014, Bozsak *et al.* aimed to explore the fluid transport behaviors of two commonly used drugs, paclitaxel and sirolimus, when released in the arterial wall by drug-eluting stents.[1] Drug-eluting stents (DESs) are devices designed to reduce narrowing of the arteries in medical procedures. This paper was aimed to improve on past computational studies with a new model that takes into account the multilayered structure of the arterial wall and the reversible (second-order) binding process of the drug, all in a three-dimensional setting.[1] These factors were not taken into account simultaneously in prior computational studies examining the same transport phenomenon.[1]

Solving the governing equations with COMSOL Multiphysics, the study modeled the DES as ten circular struts embedded in an arterial wall, with the drug being eluted from the DES along with binding reaction. The results of this computational model showed that the transport of paclitaxel in the arterial wall is predominately controlled by convention, while that of sirolimus is predominately controlled by the binding process.[1] The differences in their fluid transport dynamics in arterial walls show that drug delivery strategies must be tailored to the transport behaviors of the particular drug.[1] Additionally, it was found that accounting for the heterogeneity of the multilayered wall, which was essentially increasing the number of (homogeneous) layers from one to two, resulted in significantly different transport behaviors of the drug.[1]

3 Lab Questions

3.1 Problem 3

> Approximately how long (in seconds) does it take the system in Lab 06 to reach steady-state? Briefly justify your answer - what was your criteria for having reached steady-state?

The system took approximately $1.60 \times 10^5\,\mathrm{s} = 160\,000\,\mathrm{s}$ to reach steady-state. To determine this, the average value of antibody:antigen concentration C_s was calculated alongside the infected boundary, then plotted against time. Our rough criteria for having reached steady-state was that the concentration was unchanging, so that the concentration change over 10^5 seconds is less than $0.0050 \times 10^{-8}\,\mathrm{mol\,m^{-2}}$.

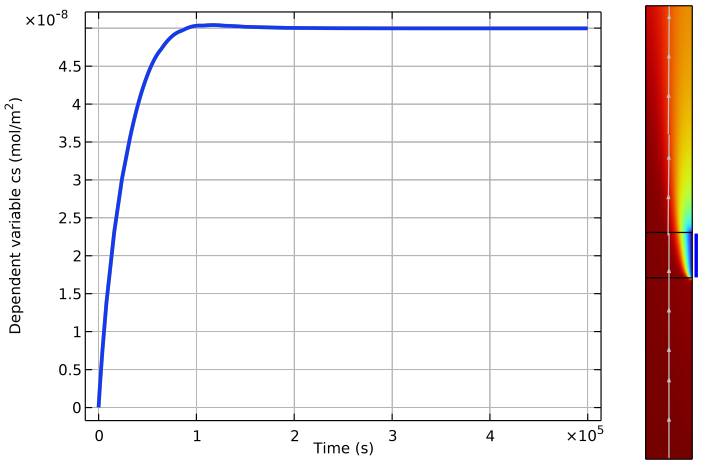


Figure 1: The average concentration (blue plot) of bound antibody:antigen along the infected boundary (also highlighted blue).

3.2 Problem 4

> What concentration (in $\mathrm{mol\,m^{-2}}$) of antibody is bound to the surface in Lab 06 at steady-state? Does that match what you would expect, given the kinetic rate constants you used in the model?

The concentration of antibody bound to the infected surface is $C_\mathrm{s} = 4.9975 \times 10^{-8}\,\mathrm{mol\,m^{-2}}$, as determined from the point graph in Figure 1. We can determine the theoretical value of C_s by considering the following reaction:

$$\text{antibody} + \text{antigen} \underset{k_\mathrm{r}}{\overset{k_\mathrm{f}}{\rightleftharpoons}} \text{antibody:antigen}$$

Let C be the concentration of antibody and C_s be the concentration of antibody:antigen complex. If a_tot was the total concentration of antigen on the vessel wall, then the

concentration of antigen at any time would be $a_{\text{tot}} - C_{\text{s}}$. At steady-state / equilibrium, the rate of the forward reaction equals the rate of the reverse reaction.

$$\begin{aligned} k_{\text{f}}[\text{antibody}][\text{antigen}] &= k_{\text{r}}[\text{antibody:antigen}] \\ k_{\text{f}}C(a_{\text{tot}} - C_{\text{s}}) &= k_{\text{r}}C_{\text{s}} \\ k_{\text{f}}Ca_{\text{tot}} &= k_{\text{r}}C_{\text{s}} + k_{\text{f}}CC_{\text{s}} \\ C_{\text{s}} &= \frac{k_{\text{f}}Ca_{\text{tot}}}{k_{\text{r}} + k_{\text{f}}C} \end{aligned}$$

From the lab spec, the values are $k_{\text{f}} = 100\,1/(\text{mol}\,\text{s}/\text{m}^3)$, $k_{\text{r}} = 0.02\,1/\text{s}$, $C = C_{\text{in}} = 1 \times 10^{-7}\,\text{mol}\,\text{m}^{-3}$, and $a_{\text{tot}} = 1 \times 10^{-4}\,\text{mol}\,\text{m}^{-2}$. We get a theoretical value for C_{s} of

$$\begin{aligned} C_{\text{s}} &= \frac{(100\,1/(\text{mol}\,\text{s}/\text{m}^3))(1 \times 10^{-7}\,\text{mol}\,\text{m}^{-3})(1 \times 10^{-4}\,\text{mol}\,\text{m}^{-2})}{(0.02\,1/\text{s}) + (100\,1/(\text{mol}\,\text{s}/\text{m}^3))(1 \times 10^{-7}\,\text{mol}\,\text{m}^{-3})} \\ &= 4.9975 \times 10^{-8}\,\text{mol}\,\text{m}^{-2} \end{aligned}$$

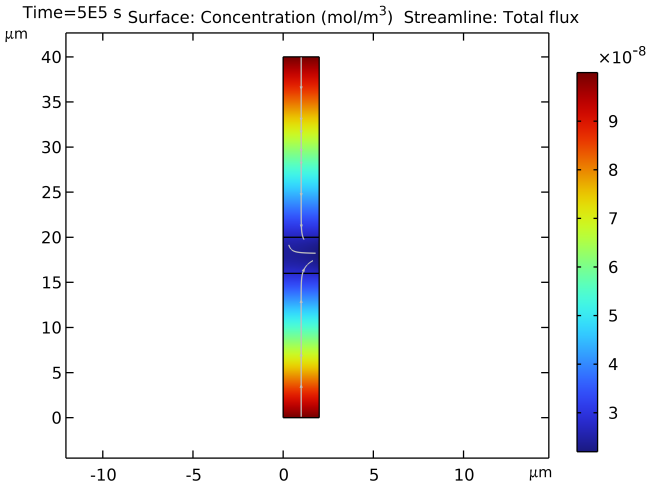
which corroborates with the experimental concentration of antibody:antigen complex.

3.3 Problem 5

> What would happen if we set flow = 0, set the initial concentration to C_{in} everywhere, and replace the inflow and outflow boundary conditions with "concentration = C_{in}"?

If the system were set up such that there is non-flowing antibody everywhere in the initial state and that there is a constant concentration of antibody at the ends of the vessel, then it makes sense that the concentration change is solely due to reaction, namely the binding between antibody and antigen.

Therefore, there is a deficiency of free antibody around the infected boundary that encompasses a larger area than in the original system, since the antibody is not flowing a certain direction.



The antibody:antigen concentration profile reaches steady-state much more slowly in the system with zero flow than in the original system. The zero velocity constraint of the fluid through the vessel results in the antigen sites binding to free antibody much less quickly, making the equilibrium state much harder to reach.

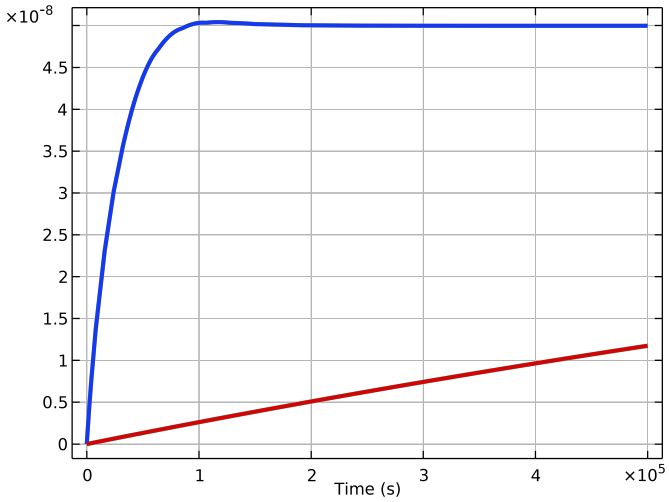


Figure 2: The average concentration of antibody:antigen over the infected boundary over time. The concentration in the system with zero flow (the red plot) is much more unchanging than the concentration in the original system (the blue plot).

References

[1] Bozsak F, Chomaz JM, Barakat AI. Modeling the transport of drugs eluted from stents: physical phenomena driving drug distribution in the arterial wall. Biomech Model Mechanobiol. 2014 Apr 1;13(2):327-47. Available from: https://doi.org/10.1007/s10237-013-0546-4.