
BE.430/2.795//6.561/10.539/HST.544

Homework Set 7

Handed out: Monday, Nov. 29, 2004

Due: Monday, Dec. 6 by 5pm

Problem 1 – Hepatocyte growth factor delivery in a rectangular bioreactor channel filled with cells

Consider the model for nutrient delivery and fluid flow through a perfused tissue bioreactor channel developed in class. In that articulation, the channel was lined with a layer of liver tissue cells and allowed the development of a parabolic axial fluid profile in the channel center. *Now, instead, consider the perfusion of a very wide, thin, rectangular bioreactor channel filled with a co-culture of vascular endothelial cells and liver tissue cells* for delivery of hepatocyte growth factor (HGF). In this case, the HGF concentration profile can be assumed to be distributed across a single rectangular coordinate axis. The tissue co-culture is established by lining the channel walls with liver cells at high density and filling the center with vascular endothelial cells at low density. Due to the presence of the endothelial cells in the channel lumen, the axial fluid velocity profile is no longer parabolic; instead it is governed by Darcy's law along the channel, relating the axial flow rate – which is uniform across the channel lumen – to the pressure gradient by a hydraulic permeability constant, (see pg 63, Deen text and pg 453, Grodzinsky notes). HGF is assumed here to be taken up only by the liver tissue cells, while diffusing through the endothelial tissue without uptake. The uptake of HGF by liver cells occurs only at the boundary between the lumen and liver cells.

- a) Derive the model equations governing the HGF concentration profile in the linear channel in terms of h (distance from channel center to liver tissue boundary), L (axial channel length), D (diffusivity of HGF through the endothelial tissue), κ , and ΔP (axial pressure gradient).
- b) The initial condition can set the HGF concentration in the fluid at the entrance to be c_i . Assuming first-order pseudo-equilibrium HGF binding, the effective HGF uptake rate at the boundary is given by

$$R_{\text{uptake}} = \left[\frac{k_e R_T n \delta}{K_D N_{Av}} \right] c$$

where k_e is the endocytosis rate constant, R_T the number of receptors per cell, n the number of cells per unit volume, δ the periphery tissue thickness, K_D the HGF/receptor affinity, N_{Av} the Avogadro's number (**derive this relation for extra-credit**). Specify the boundary conditions.

- c) Determine the HGF concentration profile throughout the linear channel by solving the equations in a) and b).
- d) For successful operation of the bioreactor, the HGF concentration at the liver tissue boundary at the bottom of the channel, should be $c_{crit} = 19$ nM. What should the minimum c_i be, such that there is sufficient delivery of HGF to the liver tissue?

Useful parameters:

$$h = 100 \mu\text{m}$$

$$L = 500 \mu\text{m}$$

$$\begin{aligned}D &= 10^{-7} \text{ cm}^2/\text{sec} \\v_m &= \kappa\Delta P = 10^3 \text{ } \mu\text{m/s} \\k_e &= 0.1 \text{ min}^{-1} \\R_T &= 10^4 \text{ receptors/cell} \\n &= 10^7 \text{ cells/cm}^3 \\\delta &= 50 \text{ } \mu\text{m} \\K_D &= 1 \text{ nM}\end{aligned}$$

Problem 2

Problem 6.4.6. (page 405) of Grodzinsky notes.