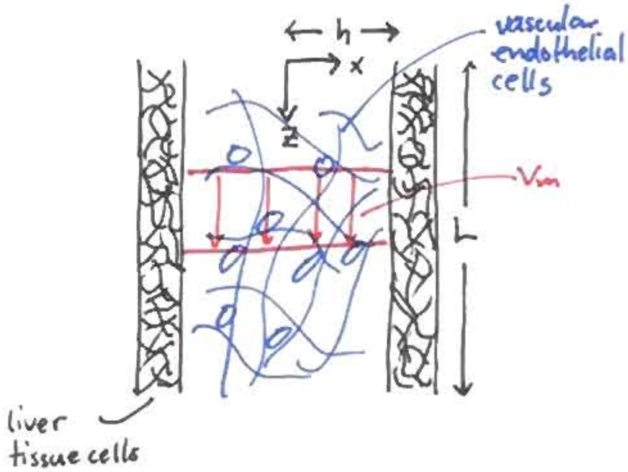
Homework #7 Problem 1 Solutions



Fluid flow in porous tissue: governed by Darcy equation

$$V_m = -K \nabla P \quad \text{with } [K] = \frac{m^4}{N \cdot s}$$

$$\left(\text{or } V_m = -\frac{K}{\mu} \nabla P \quad \text{with } [K] = m^2\right)$$

Since K, ∇P is constant, V_m is constant everywhere in the tissue.

a) Derive model equations governing HGF concentration profile.

HGF flux: $\underline{N} = -D\nabla c + \underline{V} c$

$$= -D\left(\frac{\partial c}{\partial x}\hat{i}_x + \frac{\partial c}{\partial z}\hat{i}_z\right) + (-K\nabla P)c\,\hat{i}_z$$

Conservation of HGF:

$$\frac{\partial c}{\partial t} = -\nabla \cdot \underline{N} + \cancel{R_V}^{\,0} \quad \text{no homogeneous reaction}$$

$$= D\frac{\partial^2 c}{\partial x^2} + D\frac{\partial^2 c}{\partial z^2} + K\nabla P \frac{\partial c}{\partial z}$$

We recognize that diffusion and convection processes reach steady-state in matter of seconds. Our interest of time is hours to days for our HGF delivery. So, we can safely solve the steady-state condition.

$$\Rightarrow D\frac{\partial^2 c}{\partial x^2} + D\frac{\partial^2 c}{\partial z^2} + K\nabla P\frac{\partial c}{\partial z} = 0$$

Normalize the equations: $\theta = \frac{c}{c_i}$ $\eta = \frac{x}{h}$ $\xi = \frac{z}{L}$

$$\Rightarrow \quad \frac{\partial^2\theta}{\partial\eta^2} + \frac{h^2}{L^2}\cdot\frac{\partial^2\theta}{\partial\xi^2} + \frac{K\nabla P}{D}\cdot\frac{h^2}{L}\frac{\partial\theta}{\partial\xi}$$

Let $Pe = \frac{-K\nabla P\cdot L}{D}$

$$\Rightarrow \quad \frac{\partial^2\theta}{\partial\eta^2} + \frac{h^2}{L^2}\frac{\partial^2\theta}{\partial\xi^2} \qquad \frac{h^2}{L^2}\frac{\partial\theta}{\partial\xi} = 0$$

With the given numbers,

$$Pe = \frac{10^3\,\mu m/s \cdot 500\,\mu m}{10^{-7}\,cm^2/s} = 50{,}000$$

So, we can neglect axial diffusion relative to axial convection.

$$\Rightarrow \quad \frac{\partial^2\theta}{\partial\eta^2} - Pe^*\frac{\partial\theta}{\partial\xi} = 0 \quad \text{with } Pe^* = Pe\frac{h^2}{L^2}$$

$$\Rightarrow \quad \boxed{Pe^*\frac{\partial\theta}{\partial\xi} = \frac{\partial^2\theta}{\partial\eta^2} \qquad \text{with } Pe^* = -\frac{K\nabla PL}{D}\cdot\frac{h^2}{L^2}}$$

b) Specify the boundary conditions.

Initial condition: @ $z = 0$, $c = c_i$

$$\Rightarrow \boxed{\xi = 0 , \quad \theta = 1}$$

Boundary conditions:

@ $x = 0$, $\frac{\partial c}{\partial x} = 0$ due to symmetry

$$\Rightarrow \boxed{\eta = 0 , \quad \frac{\partial\theta}{\partial\eta} = 0}$$

$$@ \quad x = \pm h \,, \quad -D\frac{\partial c}{\partial x} = \mathcal{R} = \left[\frac{k_e R_T n \delta}{K_D N_{Av}}\right] c$$

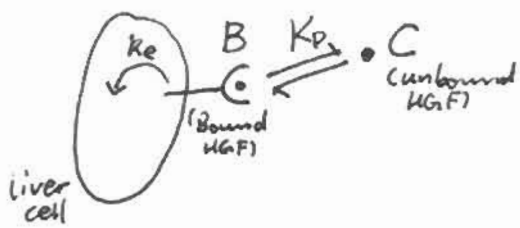
due to flux matching at liver/endothelial boundary

$$\Rightarrow \quad \eta = \pm 1 \,, \quad \frac{\partial \theta}{\partial \eta} + \frac{h}{D}\left[\frac{k_e R_T n \delta}{K_D N_{Av}}\right]\theta = 0$$

or

$$\boxed{\eta = \pm 1 \,, \quad \frac{\partial \theta}{\partial \eta} + Da \cdot \theta = 0 \qquad \text{with } Da = \frac{h}{D}\left[\frac{k_e R_T n \delta}{K_D N_{Av}}\right]}$$

Extra-credit: Derive the effective HGF uptake rate.



In pseudo-first-order equilibrium,

$$K_D \approx R_T \cdot \frac{C}{B}$$

Then, the uptake rate by the liver cell is (via endocytosis)

$$\mathcal{R}_{uptake} = k_e \cdot B = \frac{k_e R_T C}{K_D} \qquad \text{in units of cell}^{-1}\,\text{time}^{-1}.$$

To convert $\mathcal{R}_{uptake}$ into $\frac{\text{moles}}{\text{area} \cdot \text{time}}$ (units of surface flux),

$$\mathcal{R}_{uptake} = \frac{k_e R_T C}{K_D} \cdot \underbrace{\frac{1}{N_{Av}}}_{\substack{\text{Avogadro's \#} \\ (\text{mol}^{-1})}} \cdot \underbrace{\frac{\text{Volume}}{\text{area}}}_{\substack{\delta \\ (\text{m})}} \cdot \underbrace{n}_{\frac{\text{cells}}{\text{Volume}}}$$

$$\boxed{\mathcal{R}_{uptake} = \left[\frac{k_e R_T n \delta}{K_D N_{Av}}\right] C}$$

qed.

c) Solve the equations in a) and b).

$$Pe^* \frac{\partial \theta}{\partial \xi} = \frac{\partial^2 \theta}{\partial \eta^2} \qquad \text{with } Pe^* = \frac{-K \nabla P \cdot L}{D} \cdot \frac{h^2}{L^2}$$

and I.C. $\theta(\eta, \xi=0) = 1$

B.C.s $\left.\frac{\partial \theta}{\partial \eta}\right|_{\eta=0} = 0$

$$\left.\frac{\partial \theta}{\partial \eta}\right|_{\eta=1} + Da\, \theta(\eta=1, \xi) = 0 \qquad Da = \frac{h}{D}\left[\frac{k_e R_T n \delta}{K_D N_{AV}}\right]$$

Linear operator is $\mathcal{L} = \frac{\partial^2}{\partial \eta^2}$

We can solve this problem by separation of variables, Finite Fourier Transform or Eigenfunction expansion. Here, we use FFT.

① Associated eigenvalue problem:

$$\frac{d^2 \phi_n}{d\eta^2} = -\lambda_n^2 \phi \qquad \text{with} \qquad \left.\frac{\partial \phi_n}{\partial \eta}\right|_{\eta=0} = 0$$

$$\left.\frac{\partial \phi_n}{\partial \eta}\right|_{\eta=1} + Da\, \phi_n(1) = 0$$

$\Rightarrow \phi_n(\eta) = A_n \cos(\lambda_n \eta) + B_n \sin(\lambda_n \eta)$

Apply boundary conditions:

$$\phi_n'(0) = -A_n \lambda_n \cancel{\sin(\lambda_n 0)}^{\,0} + B_n \lambda_n \cos(\lambda_n 0) = 0$$

$$\Rightarrow B = 0$$

$$\phi_n'(1) = -Da\, \phi(1) \qquad \Rightarrow -A_n \lambda_n \sin \lambda_n = -Da\, A_n \cos \lambda_n$$

$$\Rightarrow \boxed{\lambda_n \tan \lambda_n = Da}$$

λ_n is defined by this equation.

For an orthonormal set of eigenfunctions:

$$\int_0^1 \phi_n^2 \, d\eta = 1$$

$$\Rightarrow \int_0^1 A_n^2 \cos^2(\lambda_n \eta)\, d\eta = 1$$

$$\Rightarrow A_n = \left(\frac{2\lambda_n}{\lambda_n + \cos\lambda_n \sin\lambda_n} \right)^{1/2}$$

So, $\phi_n(\eta) = A_n \cos(\lambda_n \eta)$

with $\lambda_n \tan\lambda_n = Da$ and $A_n = \left(\frac{2\lambda_n}{\lambda_n + \cos\lambda_n \sin\lambda_n} \right)^{1/2}$

② Define expansion & FFT

$$\theta(\eta, \xi) = \sum_{n=1}^{\infty} \bar{\theta}_n(\xi)\, \phi_n(\eta)$$

and $\langle \theta, \phi_n \rangle = \int_0^1 \theta(\eta, \xi)\, \phi_n(\eta)\, d\eta$

③ Transform the PDE & IC

PDE: $Pe^* \frac{\partial \theta}{\partial \xi} = \frac{\partial^2 \theta}{\partial \eta^2}$

Left hand side: $Pe^* \int_0^1 \frac{\partial \theta}{\partial \xi} \phi_n(\eta)\, d\eta = Pe^* \frac{\partial}{\partial \xi} \int_0^1 \theta\, \phi_n(\eta)\, d\eta = Pe^* \frac{\partial \bar{\theta}_n}{\partial \xi}$

Right hand side: $\int_0^1 \frac{\partial^2 \theta}{\partial \eta^2} \phi_n(\eta)\, d\eta = \phi_n(\eta) \frac{\partial \theta}{\partial \eta} \Big|_0^1 - \theta \frac{d\phi_n}{d\eta} \Big|_0^1 + \int_0^1 \theta \frac{d^2 \phi_n}{d\eta^2}\, d\eta$

$$= \cancel{\phi_n(1) \frac{\partial \theta}{\partial \eta} \Big|_{\eta=1} - \theta(1) \frac{d\phi_n}{d\eta} \Big|_{\eta=1}} + \int_0^1 \theta(-\lambda_n^2 \phi_n)\, d\eta$$

$$= -\lambda_n^2 \bar{\theta}_n(\xi)$$

I.C. $\bar{\theta}_n(0) = \int_0^1 \theta(\eta,0)\,\phi_n\,d\eta = \int_0^1 A_n \cos(\lambda_n \eta)\,d\eta = \frac{A_n}{\lambda_n}\sin(\lambda_n \eta)\Big|_0^1$

$= \frac{A_n}{\lambda_n}\sin\lambda_n$

④ Assemble and solve:

$$Pe^2 \frac{d\bar{\theta}_n}{d} = -\lambda_n^2\,\bar{\theta}_n(\xi) \qquad \bar{\theta}_n(0) = \frac{A_n}{\lambda_n}\sin\lambda_n$$

$$\bar{\theta}_n(\xi) = \alpha e^{-\frac{\lambda_n^2}{Pe^2}\xi}$$

$$\bar{\theta}_n(0) = \alpha = \frac{A_n}{\lambda_n}\sin\lambda_n \Rightarrow \bar{\theta}_n(\xi) = \frac{A_n}{\lambda_n}\sin\lambda_n e^{-\frac{\lambda_n^2}{Pe^2}\xi}$$

⑤ Final Solution

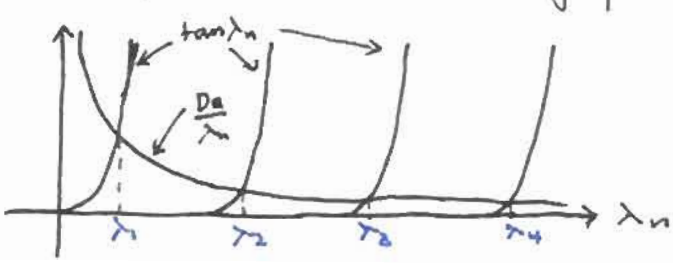
$$\boxed{\theta(\eta,\xi) = \sum_{n=1}^{\infty} \frac{A_n^2}{\lambda_n}\sin\lambda_n e^{-\frac{\lambda_n^2}{Pe^2}\xi}\cos(\lambda_n\eta)}$$

d) At the of the channel: $\xi = 1$
At the tissue boundary: $\eta = 1$

$$\Rightarrow \theta(1,1) = \sum_{n=1}^{\infty} \frac{A_n^2}{\lambda_n}\sin\lambda_n e^{-\frac{\lambda_n^2}{Pe^2}}\cos\lambda_n$$

$$\Rightarrow C_{crit} = C_i \underbrace{\sum_{n=1}^{\infty} \frac{A_n^2}{\lambda_n}\sin\lambda_n e^{-\frac{\lambda_n^2}{Pe^2}}\cos\lambda_n}_{\text{solve this sum numerically.}}$$

First, find λ_n numerically from $\lambda_n \cdot \tan\lambda_n = Da$



or

$$\tan\lambda_n = Da \cdot \frac{1}{\lambda_n}$$

$Da = 0.1384$

$$\Rightarrow \lambda_1 = 0.3637$$
$$\lambda_2 = 3.1850$$
$$\lambda_3 = 6.3051$$
$$\lambda_4 = 9.4394$$
$$\lambda_5 = 12.5774$$
$$\lambda_6 = 15.7168$$
$$\vdots$$

For $n = 300$ and $C_{crit} = 19\ nM$,

$$\underline{C_i = 19.07\ nM}$$

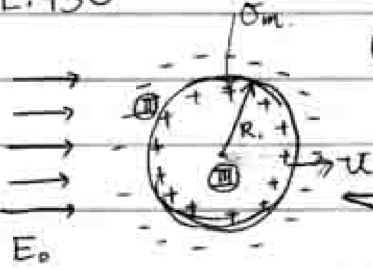
The initial concentration of influx solution should be 19.07 nM HGF. Only 0.07 nM HGF should be taken up during the transport of HGF from channel inlet to the outlet. This is due to the high Peclet number indicating that even radial diffusion process is small compared to the convection down the channel. Since not much HGF is diffusing radially, not much is taken up by the liver tissue cells. Therefore, most of HGF is retained at the bottom of the channel.

We could have simplified this problem to a 1-D linear problem with homogeneous reaction in z-direction and would have obtained similar values for c_i.

Good luck on the final exam!

BE.430 HW7 Solution

6.4.6.



① $\sigma, \varepsilon, \eta.$

$\underline{\sigma_m > 0.}$

$\sigma = \sum_i |z_i| F \mu_i c_i$

Helmholtz Model;

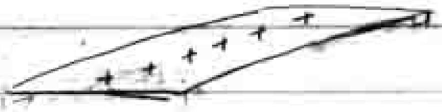
$\sigma_m = \left(\frac{\varepsilon}{d}\right)\xi.$

Helmholtz Model: $\sigma_m = \left(\frac{\varepsilon}{d}\right)\xi$

$J = \underbrace{\sigma E}_{\text{conduction}} + \underbrace{\rho_u U}_{\text{convection of charges}}$

similarly.

$K = \underbrace{-\sigma_m v_\theta^d}_{\text{Convection.}} \hat{i}_\theta + \text{conduction term.}$



$J = \sigma E$

$K = \sigma_{surface} E$

$\sigma_{surface} = \sum_i |z_i| F \mu_i c_{i\,surface}$

$= |\sigma_m| \mu$; $\mu = \mu_{Cl}$ if $\sigma_m > 0$

$\mu = \mu_{Na}$ if $\sigma_m < 0$

Eqns:

- Conservation of Charge:

  $\nabla \cdot J = n \cdot (\varepsilon E - \varepsilon E) + \nabla_\Sigma \cdot K = -\cancel{\frac{\partial \rho}{\partial t}}^{\,0}$ S.S.

- $v_\theta^d = -\frac{\varepsilon\xi}{\eta} E_\theta^d$ @ $1/\kappa$ away from surface

- $F_z^{net} = 0 = 4\pi R \mu v_\theta^d - 6\pi R \mu U$

  $U = \frac{2}{3} v_\theta^d$

$\therefore K = -\sigma_m v_\theta^d \hat{i}_\theta + |\sigma_m| \mu_{Cl} E_\theta^d \hat{i}_\theta$ where $v_\theta^d = \tilde{v}_\theta^d \sin\theta$

$= -\sigma_m v_\theta^d \hat{i}_\theta - \frac{|\sigma_m| \mu_{Cl} \eta}{\varepsilon\xi} v_\theta^d \hat{i}_\theta$

Conservation of Charge becomes:

$$-\sigma\frac{\partial \Phi}{\partial r} + \frac{1}{r\sin\theta}\frac{\partial}{\partial\theta}\left(-\sigma_m \tilde{v}_\theta^d \sin^2\theta - \frac{|\sigma_m|\mu\,\eta\,\tilde{v}_\theta^d \sin^2\theta}{\varepsilon\xi}\right) = 0.$$

① $$\frac{\partial \Phi^d}{\partial r} = \frac{1}{\sigma r \sin\theta}\left(-\sigma_m \tilde{v}_\theta^d \cdot 2\sin\theta\cos\theta - \frac{|\sigma_m|\mu\,\eta\,\tilde{v}_\theta^d \cdot 2\sin\theta\cos\theta}{\varepsilon\xi}\right)\Bigg|_{r=R}$$

$$= -\frac{2\sigma_m \cos\theta\, \tilde{v}_\theta^d}{\sigma R} - \frac{2|\sigma_m|\mu_{Cl}\,\eta \cos\theta\, \tilde{v}_\theta^d}{\sigma R \varepsilon \xi}$$

Since $\left.\begin{array}{l}\nabla\cdot\epsilon E = \cancel{\rho}^{\,0} \\ E = -\nabla\Phi\end{array}\right\}$ we have a Laplacian solution.

Guessed Solution.

$$\Phi = \frac{A\cos\theta}{r^2} - E_0 r\cos\theta$$

② $$\left.\frac{\partial\Phi}{\partial r}\right|_{r=R} = \left.\frac{-2A\cos\theta}{r^3} - E_0\cos\theta\right|_{r=R} = \frac{-2A\cos\theta}{R^3} - E_0\cos\theta$$

Setting ① & ② equal to each other:

$$\frac{-2\sigma_m\cos\theta\, v_\theta^{\sim d}}{\sigma R} - \frac{2|\sigma_m|\mu_a\eta\cos\theta\, v_\theta^{\sim d}}{\sigma R\varepsilon\xi} = \frac{-2A\cos\theta}{R^3} - E_0\cos\theta$$

$$A = \left(\frac{\cancel{2}\sigma_m v_\theta^{\sim d}}{\sigma R} + \frac{\cancel{2}|\sigma_m|\mu_a\eta v_\theta^{\sim d}}{\sigma R\varepsilon\xi} - E_0\right)\cdot\frac{R^3}{\cancel{2}}$$

$$v_\theta \simeq \frac{\varepsilon\xi}{\eta}E_\theta = -\frac{\varepsilon\xi}{\eta}\cdot\frac{1}{R}\frac{\partial\Phi}{\partial\theta} = -\frac{\varepsilon\xi}{\eta}\cdot\frac{1}{R}\left(\frac{-A\sin\theta}{R^2} + E_0 R\sin\theta\right)$$

$$v_\theta^{\sim d}\sin\theta \simeq -\frac{\varepsilon\xi}{\eta}\sin\theta\left(\frac{\sigma_m v_\theta^{\sim d}}{\sigma R} + \frac{|\sigma_m|\mu_a\eta v_\theta^{\sim d}}{\sigma R\varepsilon\xi} - \frac{E_0}{2}\right) + \frac{\varepsilon\xi}{\eta}E_0\sin\theta$$

$$v_\theta^{\sim d} = \frac{\frac{3}{2}\frac{\varepsilon\xi}{\eta}E_0}{1 + \frac{\varepsilon\xi}{\eta}\frac{\sigma_m}{\sigma R} + \frac{|\sigma_m|\mu}{\sigma R}} \;;\quad \boxed{\frac{u}{E_0} = \frac{\frac{\varepsilon\xi}{\eta}}{1 + \frac{\varepsilon\xi}{\eta}\frac{\sigma_m}{\sigma R} + \frac{|\sigma_m|\mu}{\sigma R}}}$$

b). $\frac{u}{E_0} = \dfrac{\frac{\varepsilon\xi}{\eta}}{1 + \frac{\varepsilon\xi}{\eta}\frac{\sigma_m}{\sigma R} + \frac{|\sigma_m|\mu}{\sigma R}}$

Using $\sigma_m = \frac{\varepsilon\xi}{d}$.

$u > \frac{\varepsilon\xi}{\eta}$.

$= \dfrac{\frac{\varepsilon\xi}{\eta}}{1 + \underbrace{\frac{(\varepsilon\xi)^2}{\eta d\sigma R}}_{ii} + \underbrace{\frac{\varepsilon\xi\mu\eta}{\eta d\sigma R}}_{iii}}$

although we're asked to plot $\frac{u}{E_0}$ against $\frac{\varepsilon\xi}{\eta}$, since only ξ is changing, it's valid to analyze the function with respect to ξ.

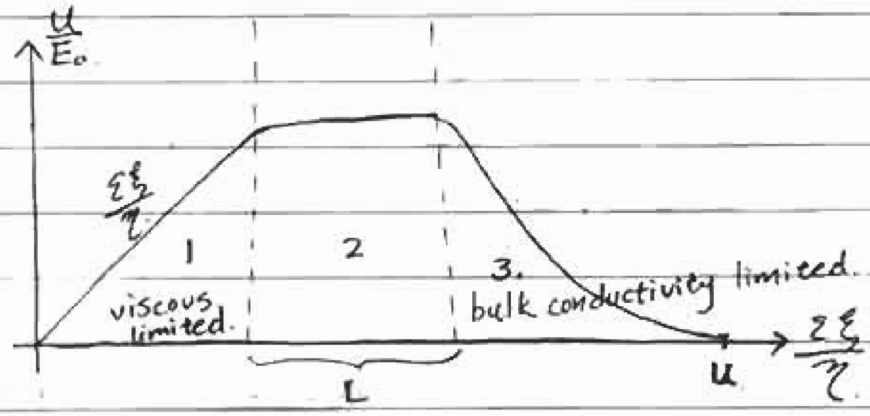
1. So, if ξ is very, very small, terms ii & iii in the denominator are negligible, $\therefore \frac{u}{E_0} \to \frac{\varepsilon\xi}{\eta}$, The physical implication is that the mobility is viscous dominated or viscous limited.

2. If iii > 1 > ii, the mobility would be flat because $\frac{u}{E_0}$ tends to $\dfrac{\frac{\varepsilon\xi}{\eta}}{\frac{\varepsilon\xi\mu\eta}{\eta d\sigma R}} = \frac{\sigma R d}{\mu\eta}$ which is a constant.

3. If i < ii < iii,

$$\frac{u}{E_0} \to \dfrac{\frac{\varepsilon\xi}{\eta}}{\frac{(\varepsilon\xi)^2}{\eta d\sigma R} + \frac{\varepsilon\xi\mu\eta}{\eta d\sigma R}} = \dfrac{1}{\frac{\varepsilon\xi}{d\sigma R} + \frac{\mu\eta}{d\sigma R}} = \dfrac{d\sigma R/\eta}{\frac{\varepsilon\xi}{\eta} + \mu}$$

In this case, $\frac{\varepsilon\xi}{\eta}$ & μ become very close such that $\frac{u}{E_0}$ tends to be bulk conductivity dominated.



L depends on parameters.