Homework 9

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BIOENG 104 Biological Transport Phenomena | Aaron Streets

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1 Problem 1

A prototypical healthy artery of diameter D_h with flow (velocity v_h) through it has a Reynolds number of Re_h. A patient arrives at the clinic with a significant amount of plaque, such that the diameter D_p of the vessel is reduced in half, with velocity v_p and Reynolds number Re_p.

(a) What is the Reynolds number Re_p in terms of Re_h (as in how much greater or smaller is Re_p)? Assume that the body attempts to keep up with the metabolic demand and keeps the volumetric flow rate constant.

From the assumption that the volumetric flow rate is constant, then

$$Q_p = Q_h \implies v_p A_p = v_h A_h$$

where Q_p and Q_h is the volumetric flow rate of the plaqued and healthy arteries, respectively. Since the cross-sectional area ratio is equal to

$$\frac{A_h}{A_p} = \frac{\pi(D_h/2)^2}{\pi(D_p/2)^2} = \left(\frac{D_h}{D_p}\right)^2 = 4 \qquad [2D_p = D_h]$$

then the average velocity of blood flow through a plaqued artery is

$$v_p = \frac{A_h}{A_p} v_h = 4v_h$$

so the Reynolds number of flow through a plaqued artery is

$$\mathsf{Re}_p = \frac{\rho v_p D_p}{\mu} = \frac{\rho(4v_h)(D_h/2)}{\mu} = 2\frac{\rho v_h D_h}{\mu} = \boxed{2\,\mathsf{Re}_h}$$

where ρ and μ are the density and viscosity of blood.

(b) How much must the diameter be occluded if the patient is to have turbulent flow in the vessel, assuming Re_h is 1000?

For turbulent flow, the Reynolds number Re_p in the patient's artery must be at least 5000. Since $\mathsf{Re} = \rho v L/\mu$ for density ρ, average velocity v, characteristic length L, and viscosity μ, then

$$\frac{\mathsf{Re}_p}{\mathsf{Re}_h} = \frac{5000}{1000} = 5 \implies \frac{\rho v_p D_p/\mu}{\rho v_h D_h/\mu} = 5 \implies \frac{v_p D_p}{v_h D_h} = 5 \tag{1.1}$$

Again assuming that the volumetric flow rate is kept constant, we have that $Q_p = Q_h$, meaning $v_p A_p = v_h A_h$, and therefore $v_p/v_h = A_h/A_p$. Calculating the cross-sectional area ratio again,

$$\frac{A_h}{A_p} = \frac{\pi(D_h/2)^2}{\pi(D_p/2)^2} = \left(\frac{D_h}{D_p}\right)^2 \tag{1.2}$$

Combining Equations (1.1) and (1.2),

$$\frac{D_p}{D_h}\left(\frac{D_h}{D_p}\right)^2 = 5 \implies \frac{D_h}{D_p} = 5 \implies \boxed{D_p = \frac{1}{5} D_h}$$

Therefore, the diameter of a healthy artery must be occluded by an 80% decrease.

> (c) What assumptions are being made in the Reynolds number, and why might turbulent flow occur with less plaque present than you calculated in part (b)?

In the calculations for the Reynolds numbers, we assumed that the patient's blood had maintained the same density and viscosity as blood in a healthy artery. Symbolically, $\rho_p = \rho_h \equiv \rho$ and $\mu_p = \mu_h = \mu$.

Additionally, when calculating for the Reynolds number, we assumed that the plaqued artery was perfectly circular. In reality, the plaque's geometry is full of irregularities, and any "clumps" of plaque are likely to disrupt the otherwise laminar blood flow. This increases the Reynolds number much farther than expected in part (b). Therefore, taking the real geometry of the plaque into account, it doesn't take much occlusion to generate turbulence in the blood flow.

2 Problem 2

> A pressure gradient drives a Newtonian fluid's flow through a cylindrical pipe with radius A. At one cross-section defined at $z = z_0$ along the length of the tube, you measure a pressure of P_1. At another cross-section, a distance L from the first, you measure a pressure of P_2. Assuming steady-state, fully-developed flow, use the Navier–Stokes equation to find the flow velocity profile, $v(r)$, in this pipe between $z = z_0$ and $z = z_0 + L$.

We make the following assumptions. First, we assume $v_r = v_\varphi = 0$, and

- that the system is at steady-state—i.e., $\partial\mathbf{v}/\partial t = \mathbf{0}$ (as given),
- that the flow is fully-developed—i.e., $\partial\mathbf{v}/\partial z = \partial\mathbf{v}/\partial\varphi = 0$ (as given),
- that the flow is also laminar, incompressible, and Newtonian (as given),
- and that any applied gravitational or electric field is negligible

The Navier–Stokes equation (NSE) states that, for an incompressible, Newtonian fluid, the velocity field $\mathbf{v}$ can be described as

$$\rho\frac{\partial\mathbf{v}}{\partial t} + \rho\mathbf{v}\cdot\boldsymbol{\nabla}\mathbf{v} = -\boldsymbol{\nabla}P + \mu\nabla^2\mathbf{v} + \rho\mathbf{g} + \sigma\mathbf{E} \tag{2.3}$$

assuming the fluid has density ρ, pressure P, viscosity μ, and charge density σ, and that a gravitational field $\mathbf{g}$ as well as an electric field $\mathbf{E}$ is applied to it. In cylindrical coordinates, the axial (z) component of the NSE can be reexpressed as

$$\rho\left(\frac{\partial v_z}{\partial t} + v_r\frac{\partial v_z}{\partial r} + \frac{v_\varphi}{r}\frac{\partial v_z}{\partial\varphi} + v_z\frac{\partial v_z}{\partial z}\right) = -\frac{\partial P}{\partial z} + \mu\left[\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial v_z}{\partial r}\right) + \frac{1}{r^2}\frac{\partial^2 v_z}{\partial\varphi^2} + \frac{\partial^2 v_z}{\partial z^2}\right] + \rho g_z \tag{2.4}$$

Our assumptions can greatly reduce the NSE into a simple differential equation,

$$\rho\left(\cancel{\frac{\partial v_z}{\partial t}} + \cancel{v_r}\frac{\partial v_z}{\partial r} + \cancel{\frac{v_\varphi}{r}}\cancel{\frac{\partial v_z}{\partial\varphi}} + v_z\cancel{\frac{\partial v_z}{\partial z}}\right) = -\frac{\partial P}{\partial z} + \mu\left[\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial v_z}{\partial r}\right) + \frac{1}{r^2}\cancel{\frac{\partial^2 v_z}{\partial\varphi^2}} + \cancel{\frac{\partial^2 v_z}{\partial z^2}}\right] + \cancel{\rho g_z} \tag{2.5}$$

turning it into

$$\frac{\partial P}{\partial z} = \frac{\mu}{r}\frac{\partial}{\partial r}\left(r\frac{\partial v_z}{\partial r}\right) \tag{2.6}$$

Since the right hand side of Equation (2.6) is a constant (say, A') with respect to z, then

$$\frac{\partial P}{\partial z} = A' \implies P = A'z + B$$

for some constant B. (I denoted A' here because A was already being used for the radius.) Solving from the other side by integrating twice,

$$\begin{aligned}
\frac{\partial}{\partial r}\left(r\frac{\partial v_z}{\partial r}\right) &= \frac{A'}{\mu}r \\
r\frac{\partial v_z}{\partial r} &= \frac{A'}{2\mu}r^2 + C \\
\frac{\partial v_z}{\partial r} &= \frac{A'}{2\mu}r + \frac{C}{r} \\
v_z &= \frac{A'}{4\mu}r^2 + C\ln r + D
\end{aligned}$$

Our boundary conditions are that

- $P(z = z_0) = P_1$ (given)
- $P(z = z_0 + L) = P_2$ (given)
- $v_z(r = A) = 0$ (no-slip boundary condition)
- $\mathrm{d}v_z/\mathrm{d}r\ (r = 0) = 0$

From the given conditions, we have

$$P_1 = A'z_0 + B$$
$$P_2 = A'(z_0 + L) + B$$

From the first equation above, $B = P_1 - A'z_0$, and therefore $P_2 = A'L + P_1$ or equivalently $A' = (P_2 - P_1)/L$. Additionally, $B = P_1 - (P_2 - P_1)z_0/L$. The (linear) pressure profile is

$$P = \frac{P_2 - P_1}{L}(z - z_0) + P_1$$

From the no-slip boundary condition, we have

$$v_z(r = A) = \frac{A'}{4\mu}A^2 + C\ln A + D = 0 \tag{2.7}$$

and from the final boundary condition, we have

$$\frac{\mathrm{d}v_z}{\mathrm{d}r} = \frac{A'}{2\mu}r + \frac{C}{r} \implies \left.\frac{\mathrm{d}v_z}{\mathrm{d}r}\right|_{r=0} = \lim_{r\to 0}\frac{C}{r} = 0$$

For the above equation to be true, C has to equal zero. From Equation (2.7), the value of D is

$$D = -\frac{A'}{4\mu}A^2 = -\frac{P_2 - P_1}{4\mu L}A^2$$

The velocity profile is

$$\boxed{v_z = \frac{P_2 - P_1}{4\mu L}(r^2 - A^2)}$$

3 Group Project Assignment

Please convene with your group to discuss the two proposals you have brainstormed. Next, locate four published manuscripts relevant to your model ideas. Submit the references for those papers with this homework.

Schedule a 20-minute consultation with either Professor Streets or one of the GSIs. Consultations can be accommodated within lab sections or office hours. Please use the Google sheet for signups (link). It is advisable to complete consultations before the due date of this homework assignment.

Proposal: Modeling the blood–brain barrier for Alzheimer's drug therapy

Over the past decades, several pharmaceutical drugs have been developed to treat brain diseases, such as Alzheimer's, Parkinson's, and brain cancers. However, the major limitation is the blood brain barrier (BBB), due to the tight junctions of the endothelial cells of the capillary network that makes up this barrier. This lack of permeability makes it difficult for drugs to reach their intended site.[1] *We aim to develop a computational model of the BBB that can help determine the necessary dosage of Memantine, a drug used to treat Alzheimer's, to achieve therapeutic concentration in the brain.*

The importance of this goal is that Alzheimer's is a disease that affects millions; thus, accurate modeling of BBB drug delivery can help determine the proper dosage levels for optimal medicinal treatment against the disease. The model will reconstruct a small capillary network representative of the blood brain barrier. Given the capillaries' dimensions, blood flow, molecular drug properties, necessary concentrations, cell properties of the barrier, and any other necessary properties, this model can help answer our question.[2] *Furthermore, taking into account known dimensions of the entire BBB network can scale our results into a realistic solution.*

However, since the BBB is a heterogeneous network of capillaries, endothelial cells, and junctional proteins, balancing the computational expense of the model and its accuracy to real-life phenomena can be a challenge. Additionally, the non-static nature of the BBB's physiological conditions is difficult to account for in a numerical simulation.

Sefidgar *et al.* (2015) details a numerical study of drug delivery in a solid tumor, generating a network of capillaries using the sprouting angiogenesis model.[2] The effects of drug delivery are deduced using fluid-flow governing equations and boundary conditions through the capillary network, framed under a static and dynamic behavior. We aim to use the same approach to roughly model the blood–brain barrier as a network of

capillaries through which the fluid flow behavior could be solved for using COMSOL.

One possible idea to use this study is to recreate the capillary network generated from angiogenesis model by tracing over it in an external CAD program, such as CATIA or AutoCAD. This is certainly not representative of all possible blood–brain barriers, but the model could earn us some insight of the real-life phenomenon regardless.

Even complex and computationally heavy models of the BBB do not take into account all dynamic factors between drug and brain membrane. Syvänen *et al.* (2006), for example, shows that decrease in drug concentration in the brain is predominantly controlled by the influx hindrance mechanism.[3] This could be intuitively viewed as a biological "partition coefficient" of the brain. The permeablility of the drug, however, has been shown to not affect the steady-state ratio but rather affect the time it takes to reach that state.[3]

Ideally, time-dependent prediction of the spatial drug distribution in the brain, and in turn the BBB, depends on the binding and pharmacokinetic properties, how the drug enters multiple intercellular transport pathways, and any metabolism that may occur between the drug and enzymes.[4]

Proposal: Modeling intraocular drug delivery

Sight-threatening diseases have become more prevalent among individuals affected by factors of age and choice of lifestyle. Many such diseases require a drug delivery pathway (e.g. injection) to the posterior segment directly into the vitreous.[5] *Hence,* in vitro *and* in silico *modeling studies of optimal intravitreal injection of drugs is essential for understanding ocular drug delivery and improvement of therapeutic strategies. However, some challenges come in the form of computational modeling, since the multiple cellular layers existing in the outer blood barrier should be considered along with its physical and geometrical intricacies. Another caveat is choosing an appropriate physiological model system (*in vitro *or* in silico*) which accurately reflects the outer-blood-retinal barrier characteristics of a particular subsect of species or disease. A practical challenge therefore is the cost and invasive nature of intravitreal injection itself. For this project, a simplified structure of the eye will be constructed in COMSOL to model intraocular drug delivery to the vitreous of the eye. By utilizing a time-dependent and "transport of diluted species in a porous media" study, it will be possible to calculate the required time to transmit an effective dosage from a drug delivery patch releasing a given concentration per second. To mitigate the complexities of the cellular layers, three tissue layers will be constructed around a sphere, representing the vitreous humor.*[6] *With known material properties and transport properties, a specific time value will be produced as a solution.*[7,8]

For scheduling purposes:

- Group name: I
- Date/Time: Thursday, March 21, 1:50–2:10pm

References

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