Homework 1
Due Wednesday (9/22) by 5pm

1. **Oxygen Diffusion in Cells**

   a) Oxygen is consumed by cells at a rate which is often nearly independent of the O_2 concentration. Assume that a cell is a sphere of radius a, and let k_0 and C_0 be the O_2 consumption rate per unit volume and the O_2 concentration just inside the cell membrane, respectively. Derive an expression for the steady-state O_2 concentration profile in the cell, $C(r)$, assuming that the consumption rate is spatially uniform. Using the data given below, show that diffusion limitations at the single-cell level are unimportant.

   Data: $D_c = 1 \times 10^{-5} \frac{cm^2}{s}$ (O_2 diffusivity in cytoplasm)

   $\dot{m}_c = 0.2 \frac{pmol}{h \cdot cell}$ (typical O_2 consumption rate of mammalian cell)

   $a \leq 10 \mu m$

   $C_0 = 60 \mu M$ (typical O_2 level in mixed venous blood or tissues)

   b) Consider now an aggregate of closely packed cells which is a sphere of radius b ($>>a$). If b and k_0 are sufficiently large, no O_2 will reach a "central core." In the central core the assumption of zeroth-order kinetics is no longer valid, because no O_2 is available to react. Assuming that the diffusional resistance of the cell membranes is negligible (i.e., regarding that aggregate as a homogenous fluid), derive an expression which indicates when a central core will exist. [This situation occurs in certain solid tumors. If the tumor develops without a sufficient internal blood supply, the cells in the center are killed by hypoxia.]

2. Chemoattractant Generation by a Spherical Tumor

Consider the model for the situation of a chemoattractant concentration profile generated at steady-state in 3-dimensional tissue of essentially infinite extent from a spherical tumor. Assume that there is no reactive loss of the chemoattractant in the tissue. For a typical situation of this sort, the following parameter values might be reasonable estimates:

- chemoattractant diffusivity $\square\ 3\times10^{-7}\ \frac{cm^2}{s}$
- tumor spheroid radius ~ 300 μm
- chemoattractant generation rate ~1000 $molecules/cell\cdot min$
- cell radius ~10 μm

a) Calculate the concentration, c(x), and the concentration gradient of chemoattractant, $\frac{dc(x)}{dx}$, as functions of distance away from the tumor spheroid in the tissue. Ascertain what region in the tissue the blood vessel endothelial cells would be able to adequately perceive the chemoattractant gradient, provided that this perception requires a local concentration in the range $0.3\times10^{-9}M \square\ 3\times10^{-9}M$.

b) Develop a design for an in vitro assay aimed at creating a 1-dimensional steady-state chemoattractant concentration profile capable of inducing chemotacting migration of the endothelial cells.

3. Deen 2.11

4. Deen 2.12