Problem Set 3 **BE.462J/3.962J**
Issued: Day 6 **Spring 2003**
Due: Day 8
(20 pts total)

A recent study of controlled release of a model small-molecule drug from poly(lactide-co-glycolide) microspheres prepared by the single-emulsion method found that the diffusion constant of the drug through the polymer was best related to the polymer's molecular weight according to:

$$D(t) = D_0 + \frac{\phi}{M(t)}$$

In this equation, ϕ and D_0 are constants, and M(t) is the molecular weight of the matrix polymer. From data obtained on PLGA microspheres, the constants were determined to be:

$\phi = 2.1 \times 10^{-11}$ cm^2(kg/mole)/s
$D_0 = 4.9 \times 10^{-12}$ cm^2/s

We can use this expression for D(t) in the Charlier controlled release model to obtain modified expressions for h(t) and Q(t) (we'll call this model B, and the expression derived in class model A). Assume that the molecular weight $M(t) = M_0 e^{-kt}$, where M_0 is the initial molecular weight and k is the degradation rate constant for PLGA hydrolysis. A reasonable estimate for k is:

Degradation rate constant for PLGA hydrolysis: k = 9.8E-03 hr^{-1}

1. (5 pts) Quantitatively, will the diffusion constant in model B given above differ significantly from that obtained from model A derived in class over experimentally-relevant timescales?

2. (5 pts) Using the model B formula above for the diffusion constant, derive a new expression for the thickness of the diffusion field h(t) in the Charlier model. Assume M(t) has an exponential decay with time as derived in class.

3. (10 pts) Using the data above and that given below, determine how long release experiments that measure Q(t) (total amount of drug released at time t) would need to be carried out to distinguish which of the two models for the diffusion constant ($D = D_0 e^{kt}$ as derived in class, or the expression given above) best represents release of HGH from a PLGA matrix in the framework of the Charlier model. (Hint: plot Q(t) for each of the two models; solve for Q(t) in model B by numerically integrating an expression dQ = (…)dt.)

Solubility of HGH in PLGA matrix:	$C_s = 6.12E\text{-}04$ g/cm^3
Concentration of HGH encapsulated in the matrix:	$C_0 = 0.02$ g/cm^3
Surface area of release matrix:	A = 1.67 cm^2
Initial molecular weight of the matrix:	$M_0 = 78{,}000$ g/mole