Appendix B

Diffusion Modeling

B.1 PDGF Modeling

The PDGF signaling parameters are taken from an analysis performed by Lauffenburger *et al.* [71]. The threshold sensing concentration is based on the dissociation constant of PDGF given as, $K_d = 10^{-10}$ - 10^{-9} [mol/L]. The production rate, q_{PDGF}, is given as 10^{-16} - 10^{-15} [g/cell/min] which was cited as being taken from Leof *et al.* [74], a study using human foreskin fibroblasts. The molecular weight was estimated to be 30 [kDa]. Using the molecular weight we can convert the units of q_{PDGF} to yield 5e-16/(30000*60) = 2.78e-22 [mol/cell/s]. The Einstein-Stokes equation gives $D = 79$ [μm^2/s] for the 30 [kDa] molecule.

B.2 EGF Modeling

EGF modeling was taken from work by Knauer *et al.*[65] and Starbuck *et al.*[119]. This work is based on data obtained using human and mouse fibroblasts. The EGF complex internalization rate constant, k_{eC}, was measured to be 5.3e-3 [s^{-1}]. Half maximal response occurs at 0.15 [ng/mL] and 2000 surface complexes per cell. This means an internalization rate of 2000*5.3e-3 = 10.6 [molecules/cell/s]. The molecular weight of EGF and the EGF/EGF binding protein complex were cited as 6.4 and 74 [kDa] respectively. Converting units we get a 10.6/6.022e23 = 1.76e-23 [mol/cell/s] EGF uptake rate for fibroblast cells. Thus, q_{max} = 2*1.76e-23 = 3.52e-23 [mol/cell/s]. Cellular affinity for EGF is about 4.69e-11 [mol/L] vs. a K_d of 4.7e-9 [mol/L].

Again, using the Einstein-Stokes equation, a 6.4 [kDa] molecule gives a diffusion coefficient of D = 131 [µm^2/s] and 58 [µm^2/s] for a 74 [kDa] molecule. The latter is used to estimate the diffusing protein.

Factor uptake, q, is assumed to follow the Michaelis-Menten kinetics with respect to the concentration of a rate limiting factor (Eq B.1). The value q_{max} represents the maximum uptake rate per cell. C_{cb} is the concentration of factor at the cell boundary and C_{th} is the Monod or Michaelis-Menten constant. Per the definition of the Michaelis-Menten constant (Eq B.1), when $C_{cb} = C_{th}$ then $q = q_{max}/2$. Thus, we use the threshold sensing concentration for the Michaelis-Menten constant. Therefore, when concentration at the cell boundary is 0, there is no uptake of factor, while at C_{th}, uptake is $q_{max}/2$.

$$q = \frac{q_{max} C_{cb}}{C_{th} + C_{cb}} = \frac{q_{max}}{1 + \frac{C_{th}}{C_{cb}}} \tag{B.1}$$