Spring 2014 Cellular Bioengineering In-Class Group Problems on R-L binding

1) Many receptors dimerize (bind to each other). Many of them can do so whether or not the respective receptor components have ligand bound to them.
   a) Draw all of the possible components and name them.
   b) Write/Draw all of the possible interactions – with labels on everything.
   c) Write the rate equations and the receptor balance.

2) Vascular endothelial growth factor (VEGF) is an important growth factor in angiogenesis, the formation of new blood vessels. Promoting and inhibiting VEGF signaling has been extensively studied in areas such as wound healing and cancer biology. Like many biologically active molecules, VEGF (VEGF-A specifically) has two main receptors (cleverly known as VEGFR-1 and VEGFR-2, or FLT-1 and KDR, respectively). VEGF-2 is thought to be responsible for the angiogenic effects, while it has been suggested that one role of VEGF-1 in vessel maturation is to sequester VEGF.
   a) Schematically draw and label VEGF binding to its receptors.
   b) Write rate equations for bound VEGF
   c) Write mass balances for all compounds
   d) If we were interested in studying sequestration, what assumptions would we make and/or what experimental precautions would we need to take?
   e) Solve the equations for something we can measure in terms of known variables. Assume excess ligand and steady state.
   f) Let's play with graphing!
      i) Assume that the dissociation constants for VEGFR-1 and VEGFR-2 are ~10 pM and ~0.5 pM and that the maximal local VEGF concentration is ~10 pM.
      ii) The cells we're interested in are estimated to have 3000-9000 VEGFR-1 and 40,000-120,000 VEGFR-2 per cell.
      iii) Graph ligand vs. complex for each complex type. Look at how changing the maximum VEGF concentration alters the appearance of the graph. What are the experimental implications?
      iv) Make Scatchard plots for each complex type. Look at how changing the total number of each receptor type affects the plot.