Problem H2 How tight can Binding of one protein to another be?

Use Livnah.pdf, and Stroud lecture notes

1. Design an experiment to produce a therapeutic small peptide-based agent to activate the response against certain bacterial infections, mediated normally by the cytokine IL-6, via its receptors IL-6R, and gp130. Activation of the response is brought about by bringing these two receptors together on cell surfaces. This system is very related to that of the EPO – EPO receptor system except that there are two different receptor chains, whereas in EPOR they are both identical.

Expression of as many as $10^{10}$ different variants of a given protein or peptide, coupled with selection according to those that bind a given target most tightly can be used to ask biology to design the best mating surface for a nominated protein. EPOR is a transmembrane receptor activated by bringing two identical receptor chains together as a dimer on the cell surface to activate internal kinase pathways.

2. What do we know about the components that lead to the tightest binding peptide discovered in the particular template chosen for the EPO experiment? Hydrophobic binding energy gives $\sim -22\text{cal/Å}^2$ on each hydrophobic surface buried in a protein-protein interaction. A hydrogen bond between uncharged species is worth $\sim -1\text{kcal/Mole}$. Use the data in Fig 4 & Table 2 to estimate the binding energy $\Delta G^0$ for the capture of one EPOR to the complex of EBP-2EMP. What will you estimate the dissociation constant $K_d$ to be for this interaction? Therefore at what concentration of EBP will this complex be 50% dissociated?