Name:

GPCRs and Modulation homework

1. Please name two effectors for the following G Protein classes: (6 pts)
    a. $G_{i/0}$

    b. G_s

    c. $G_{q/11}$

2. What are 5 ways a GPCR can affect the communication between two neurons? (10 pts)

3. Pick one effector of one G Protein activated by a GPCR and describe the signaling cascade in detail. Use a diagram if desired. (10 pts)

4. You are recording a response in your cell to the brief application of acetylcholine, which activates metabotropic and ionotropic receptors. How can you test if the response you're recording is through a GPCR? (15 pts)

5. After some testing you think the ACh response is through a GPCR. But muscarinic receptors can be either $G_{i/o}$ or G_q subtypes. How would you distinguish between these? (15 pts)

6. Define receptor desensitization (4 pts)

7. How do GPCRs desensitize? (10 pts)

8. Describe, in order, the G protein cycle. Indicate one way to modulate this cycle. (10 pts)

EXTRA CREDIT!!! These questions are fun and challenging, but only do them if you have the time and the desire.

1. For a GPCR, is the K_d (receptor binding affinity) the same as the EC_{50} (a measurement that depends on measuring the effect of receptor activation)? Why or why not? (10 pts)

2. How could you modulate the EC_{50} without affecting the K_d? (10 pts).

3. GPCR signaling pathways can be divided into *membrane delimited pathways* that rely entirely on proteins attached the plasma membrane and *freely diffusible second messengers* that signal through the cytosol. How would you design an experiment to test if what you're measure is *membrane delimited* or *freely diffusible*?

4. GIRK channels rely on the phospholipid $PI(4,5)P_2$ (PIP2) for channel function. You find that a G_q GPCR decreases GIRK activity. What might be happening here? How would you test it?

5. Where does the name metabotropic come from? Why is that important?

6. Early studies in the mechanism of adenlyate cyclase activation found that the α subunit is required for activation, but that the $\beta\gamma$ subunits also affect the activity though inhibition. What are TWO ways the $\beta\gamma$ subunits could inhibit AC activity?