

The surface of a cell has a receptor where ligands become attached.

- A.** For antigen-detecting receptors like the T Cell Receptor, these ligands come in two types: agonists and antagonists. Assume that molecules arrive according to a Poisson process with rate  $\lambda$ . Among these molecules, a proportion  $\alpha$  are agonists (so  $0 \leq \alpha \leq 1$ ) and the rest are antagonists. Antagonists remain attached for an exponentially-distributed duration with parameter  $\mu_1$ , while agonists remain attached for an exponentially-distributed duration with parameter  $\mu_2$ . An arriving molecule only becomes attached if the receptor is free of other molecules.

What is the percentage of time the receptor is occupied by an agonist? By an antagonist? Free?

- B.** For this part, assume there is only one type of ligand. The ligand binds to the receptor at rate  $\lambda$  and unbinds at rate  $\mu$ . Once the ligand is bound, the receptor initiates an intracellular signal at rate  $k$ , but it can only do this while a ligand is bound.

- (a) Write a 3-state continuous-time Markov transition matrix to describe this process.
- (b) Suppose that at time  $t = 0$ , there is a ligand bound to the receptor. How long on average until a signal is transduced?
- (c) **[OUT-OF-CLASS]** Suppose that the receptor's kinetics are controlled by a control variable, so that  $\lambda = c\lambda^*$  and  $\mu = c\mu^*$ . Again suppose the system starts with a ligand bound. Assume receptor kinetics have been slowed to approximately zero speed, so  $c = 0$ , i.e.,  $\lambda = \mu = 0$ . In other words, the ligand is very unlikely to ever unbind.
  - i. According to your intuition, what is the mean time until a signal is transduced?
  - ii. Set  $\lambda = \mu = 0$  in the transition matrix. What is the mean time until a signal is transduced? Does this agree with your intuition?
  - iii. Set  $\lambda = \mu = 0$  in your answer from Part (b). What is the mean time until a signal is transduced? Does this agree with your intuition?