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 λ. Among these molecules, a proportion α are agonists (so $0 \leq \alpha \leq 1$) and the rest are antagonists. Antagonists remain attached for an exponentially-distributed duration with parameter μ_1, while agonists remain attached for an exponentially-distributed duration with parameter μ_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 λ and unbinds at rate μ. 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 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) Suppose that the receptor's kinetics are controlled by a control variable, so that $\lambda = c\lambda^\star$ and $\mu = c\mu^\star$. 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?