1. Why are both amplification and adaptation required for chemotaxis? Consider a bacterium as it successfully navigates up a gradient in chemoattractant.
   1. Amplification allows for switch like behavior, while adaption brings the system back to the amplification threshold of the switch after each stimulus. Taking a bacterium navigating a chemical gradient of chemoattractant as an example, the bacterium needs to react to a small change in concentration to know which direction to swim. Therefore, a small change in ligand concentration has to be amplified and cause a reaction by the cell. When the cell gets to a new location, it needs to sense another change in ligand concentration to know where to swim. If the bacterium receptors are passed the region of switch-like sensitivity, it will not be able to react to a concentration gradient and swim in that direction. Therefore, the bacterium requires adaptation to revert the cell’s reaction/amplification system back to the region of switch-like sensitivity, so the bacterium can sense the next concentration change and swim in that direction.
2. What are the mechanisms for amplification in the proposed models of this signaling pathway? Consider the level of description of the network that is shown in Box 1 of Alon et al.
   1. Inhibition-driven amplification
   2. Chemotactic attractants are sensed by the receptor which then forms a complex and transitions between an activate and inactive state. The active state and inactive state can be methylated. The amplified outputted signal is the total amount of methylated active receptors.
3. What are the mechanisms of adaptation in the proposed models?
   1. The adaptation brings the system back the threshold of switchlike response to stimulus. This is due to the reverse modification of the receptor which compensates for the effects of the ligand binding to the receptor. The mechanism also ensures that at steady state there are an excess of non-bound/uninhibited receptors that are active.
4. What is the “robustness” with which Barkai et al. are concerned and why?
   1. The function of the biological system is independent of the exact biological parameters that vary from cell to cell. For example, this means that the biological parameters do not need to be fine-tuned to achieve the amplification-adaption function. This is important because there will naturally be fluctuations in the rate constants, binding constants, etc. from stochastic variation, but all of the related cells need to perform the same function.