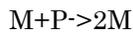


BP205 Molecular Dynamics of the Cell
Problem Set 4
Due February 10th in class

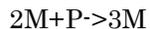
1. Prion Autocatalysis

Prions are aggregates of misfolded proteins that grow by interacting with properly folded proteins, forcing them into a misfolded state. We'll model prion formation by assuming that the protein in a cell exists in two states, misfolded and properly folded, which we'll call M and P, respectively. Misfolded proteins are formed through the following reaction, which occurs at rate k :



Assume that M and P both degrade at the same rate, and that P is constantly produced at a rate that is equal to some constant, P_0 , times the degradation rate.

- Write out de-dimensionalized differential equations describing the rate at which both M and P are produced and degraded.
- Download the file "Autocatalysis.ode" from the course web page. Use this file and AUTO to plot the steady states of this system as the de-dimensionalized reaction rate (called kappa in the .ode file), is varied between 10 and 100. Are there any values of kappa for which the final prion concentration depends on the initial state of the system?
- Now, assume that the creation of each new misfolded protein requires the action of two already misfolded proteins:



Write out the de-dimensionalized differential equations that will describe the dynamics of the system in this case. Use AUTO to plot steady state as the de-dimensionalized reaction rate varies over the range of 10 to 100. In this case, are there any values of kappa for which the final prion concentration depends on the initial state of the system?

2. Transcriptional time scales

Bacterial transcription requires the association of core RNA polymerase with a sigma subunit that is responsible for promoter recognition and melting. Transcriptional initiation in individual promoters in bacteria occurs on the time scale of seconds.

- A cell has sigma subunits and core RNAP both at concentration 10 μ M. Assume that sigma and core RNAP have affinity of 1 nM for each other, and that their association is diffusion limited and happens with a forward kinetic rate $k = 10^6 \text{ M}^{-1}\text{s}^{-1}$. Over what time scale will sigma-core interactions reach equilibrium? Is it fair to model sigma and core as being in equilibrium in a model of transcription?
- Non-specific interactions between RNA polymerase and DNA can influence the rate of transcriptional initiation in bacteria. Assume that DNA replication proceeds at 800 base pairs/sec, and the bacterial genome consists of 6,000,000 base pairs – how does the time scale of DNA replication compare with that of transcription initiation?