HW 8: Noise and stochastic chemical systems.

(Dated: November 29, 2010)

1. A PROGRAMMING LANGUAGE FOR COMPOSABLE DNA CIRCUITS.

The paper "A programming language for composable DNA circuits" by Luca Cardelli and Andre Phillips contains a formal description of the DNA strand displacement systems discussed in class.

(a) Using that programming language, write a code that specifies the AND gate (and inputs). Run your program on Visual DSD (google visual DSD, you may have to install Silverlight.) There are lots of examples for programs available at Visual DSD. Take a screen shot of the reaction kinetics plot, the species and reactions generated by the code.

(b) What are the key assumptions/approximations used in the Visual DSD language and model?

2. MODELING GENE EXPRESSION.

mRNA and protein synthesis occurs in bursts. Bursts of mRNA synthesis can be modeled if it is assumed that the gene/promoter switches between an active and an inactive state:

$$I \xrightarrow{\lambda} A \tag{1}$$

$$A \xrightarrow{\gamma} I \tag{2}$$

$$A \xrightarrow{\mu} A + M \tag{3}$$

$$M \xrightarrow{\delta} \emptyset \tag{4}$$

Here, A is the active gene, I is the inactive gene and M is the mRNA.

(a) What possible mechanisms could lead to transitions between active and inactive states? (Find a review on noise in gene expression for help with this answer).

(b) Derive the master equation for this system following the ideas introduced in class. (For extra points, solve it analytically. This is hard.)

(c) Implement the model using Gillespie's algorithm. Use the rate constants from "Stochastic mRNA Synthesis in Mammalian Cells" by A. Raj *et al.* PLOS Biology **4**, e309 (2006) (some of the numbers may be hidden in figure captions and supplementary info). Information of typical mRNA counts/cell can also be found in that paper.

3. STOCHASTIC AND DETERMINISTIC MODELS.

Consider the following system of chemical reactions:

$$A + B \xrightarrow{k} 2B \tag{5}$$

$$B + C \xrightarrow{k} 2C \tag{6}$$

$$C + A \xrightarrow{k} 2A \tag{7}$$

(a) Derive and implement the corresponding chemical reaction equations. Find a set of parameters and initial values for which this system oscillates.

(b) Model the same system using Gillespie's algorithm.