Homework # 3 (Due Friday, Oct. 28)

1. We shall again consider the same nonlinear (bio)chemical reaction system as in Homework # 2:

$$A + 2X \underset{\beta}{\overset{\alpha}{\rightleftharpoons}} 3X, \quad X \underset{\delta}{\overset{\lambda}{\rightleftharpoons}} B.$$

But this time, the reaction system is in a very small system with volume V, and we shall consider the dynamics in terms of the number of X molecule at time t. The $n_X(t)$ is integer-valued, continuous-time Markov process, defined on $\mathbb{Z}$. We keep the convention that A and B are chemical species with *maintained*, constant concentrations a and b. In these terminologies, the concentrations of X is also stochastic processes with discrete values $\dfrac{n_X(t)}{V}$.

(a) Write the Chemical Master Equation (CME) for the reaction system: i.e., a system of ordinary differential equations for the probability $p_m(t) = \Pr\{n_X(t) = m\}$.

(b) Write a short computer code to carry out a Monte Carlo simulations of the stochastic dynamics. The method is widely known as the Gillespie algorithm. Let volume $V = 100$, using the set of parameters: $\alpha = 3c^{-2}t^{-1}$ where c denotes the unit for "concentration" and t denotes the unit for "time", $\beta = 0.6c^{-2}t^{-1}$, $\lambda = 2.95t^{-1}$, $\delta = 0.25t^{-1}$; $a = 1c$ and $b = 1.5c$, run a long simulation and collect the histogram for the time the system taking values $N_X(t) = n$. Note that Gillespie algorithm has non-uniform time steps.

(c) Repeat the (c) again using the parameter set $\alpha = 3c^{-2}t^{-1}$, $\beta = 0.6c^{-2}t^{-1}$, $\lambda = 2.95t^{-1}$, $\delta = 0.25t^{-1}$; $a = 1c$ and $b = 59c$.

(d) Alternatively, you can obtain the stationary distributions for $p_n(t)$ from the CME you obtained in (c). Compare the analytical results with the simulations.

2. We shall again consider the nonlinear chemical reaction system:

$$A + 2X \underset{\beta}{\overset{\alpha}{\rightleftharpoons}} 3X, \quad X \underset{\delta}{\overset{\lambda}{\rightleftharpoons}} B.$$

We keep the convention that X and Y are *dynamic chemical species* and A and B are chemical species with *maintained*, constant concentrations. Use lower cases x, y and a, b for the concentrations of the corresponding chemical species.

(a) Following the *Law of Mass Action*, write the ordinary differential equation (ODE) for the chemical reaction system.

(b) Show that if the concentrations of A and B are at their chemical equilibrium, i.e.,

$$\frac{a \times \alpha \times \lambda}{b \times \delta \times \beta} = 1,$$

then the chemical dynamics following the equation in (a) has only a single fixed point. In fact, the fixed point is a chemical equilibrium.

(c) Even though there are six parameters in the model, show that if we use the non-dimensionalized concentration $\hat{x} = (\lambda x/\delta b)$ and non-dimensionalized time $\hat{t} = \lambda t$ as new variables, then the ODE from (a) can be simplified into

$$\frac{\mathrm{d}\hat{x}}{\mathrm{d}\hat{t}} = -\theta\hat{x}^3 + \mu\hat{x}^2 - \hat{x} + 1 = f(x, \mu, \theta), \tag{1.14}$$

where the two positive parameters are

$$\mu = \frac{\alpha\delta ab}{\lambda^2} \quad \text{and} \quad \theta = \frac{\beta(\delta b)^2}{\lambda^3}.$$

(d) Show that the curve in (θ, μ) plane, which divides it into regions where there are 1 or 3 positive steady states is given parametrically by

$$\theta = \frac{\xi - 2}{\xi^3}, \quad \mu = \frac{2\xi - 3}{\xi^2}.$$

Show that the two curves meet at a cusp, where $\mathrm{d}\theta/\mathrm{d}\xi = \mathrm{d}\mu/\mathrm{d}\xi = 0$ at a critical ξ^*. Sketch the curve in (θ, μ) plane.

3. This is an open-ended problem.

(a) Repeat the computaions in Problem 1 with increasing number of molecules and increasing volume V such that $n_X(t)/V$ becomes smoother and smoother. Convince yourself in the limit of $V \to \infty$, your simulation results agree with the predictions from the ODE in Problem 2.

(b) Try to obtain the stationary distribution of the problem with finite V, then let $V \to \infty$. In other words, taking the limit $V \to \infty$ after $t \to \infty$. Do you think this will give you the same answer as $t \to \infty$ after $V \to \infty$? If not, what do you expect to see? Try to use analytical mathematics or computations as tools for this question.