

Math 289 Notes, 10/29/08

October 30, 2008

1 Biochemical Reaction Networks

$(\mathcal{S}, \mathcal{C}, \mathcal{R})$, where $\mathcal{S}$ is a finite set of species $\{A_1, \dots, A_n\}$, $\mathcal{C}$ is a finite set of complexes (left and right hand sides of reactions) $\{\nu \in \mathbb{Z}_+^n\}$, and $\mathcal{R}$ is a finite set of reactions $\{\nu \xrightarrow{\kappa} \nu'\}$.

2 Markov Chain Model

$$X(t) = \begin{pmatrix} X_1(t) \\ \vdots \\ X_n(t) \end{pmatrix}, \quad t \geq 0,$$

where $X_i(t)$ is the number of molecules of species i available at time t .

Let $N_1, \dots, N_K$ be independent rate one Poisson processes where K is the number of reactions. Then we have the ‘microscopic stochastic model’:

$$X(t) = X(0) + \sum_{k=1}^K N_k \left(\int_0^t \lambda_k(X(s)) ds \right) \cdot (\nu'_k - \nu_k)$$

3 Mass Action Kinetics

For the k^{th} reaction, $\nu_k \xrightarrow{\kappa_k} \nu'_k$, with mass action kinetics,

$$\lambda_k(x) = \kappa_k \prod_{i=1}^n \nu_{ik}! \binom{x_i}{\nu_{ik}}$$

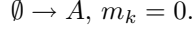
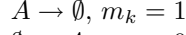
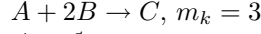
where x_i is the number of molecules of species i currently available, $i = 1, \dots, n$.

If V is the volume for the system, Gillespie’s argument gives that

$$\kappa_k \propto \frac{1}{V^{m_k-1}}$$

where $m_k = \sum_{i=1}^n \nu_{ik}$, the number of molecules consumed in reaction k .

Example.



Assume that for each k , $\kappa_k = \frac{\tilde{\kappa}_k}{V^{m_k-1}}$ where $\tilde{\kappa}_k$ is independent of V .
Assume that $r = V$ goes to ∞ through a sequence, i.e, $r_m \rightarrow \infty$ as $m \rightarrow \infty$.

4 Sequences of Networks

Now, $\lambda_k^r(x) = r \tilde{\kappa}_k r^{-m_k} \prod_{i=1}^n x_i (x_i - 1) \cdots (x_i - \nu_{ik} + 1)$. Thus, setting $c_i = \frac{x_i}{r}$ for $i = 1, \dots, n$, we have

$$\lambda_k^r(x) = r \tilde{\kappa}_k \underbrace{\prod_{i=1}^n \left\{ c_i \left(c_i - \frac{1}{r} \right) \cdots \left(c_i - \frac{(\nu_{ik} - 1)}{r} \right) \right\}}_{f_k^r(c)}$$

In the r th system,

$$\bar{X}^r(t) = \frac{X^r(t)}{r} = \frac{X^r(0)}{r} + \sum_{k=1}^K \frac{1}{r} N_k \left(\int_0^t r f_k^r(\bar{X}^r(s)) ds \right) (\nu'_k - \nu_k)$$

Assume that $\bar{X}^r(0) \Rightarrow \bar{X}_0$ as $r \rightarrow \infty$ where $\bar{X}_0$ is a finite random variable.

Now $\{\bar{X}^r\}$ is a sequence of processes in $\mathbb{D}([0, \infty), \mathbb{R}_{\geq 0}^n)$, where $\mathbb{R}_{\geq 0}^n$ is the n -dimensional closed positive orthant.

5 Criterion for C -tightness

Recall that $\{\bar{X}^r\}$ is C -tight if for each $T > 0$, $\epsilon > 0$, there exist $\delta^* = \delta(\epsilon, T)$, $K^* = K(\epsilon, T)$ and $r^* = r(\epsilon, T)$ such that for all $r \geq r^*$,

- (i) $P(\|\bar{X}^r(\cdot)\|_T \geq K^*) < \epsilon$ (compact containment)
- (ii) $P(w(\bar{X}^r, \delta^*, T) \geq \epsilon) < \epsilon$ (control of oscillations).

6 Strong Approximation

By the strong approximation result, we can choose the probability space on which $N_1, \dots, N_K$ are defined such that it also supports independent standard one-dimensional Brownian motions $W_1, \dots, W_K$ where

$$\eta_k(t) \equiv \frac{N_k(t) - t - W_k(t)}{\log(t) \vee \sqrt{2}}, \quad t \geq 0, k = 1, \dots, K$$

satisfies $\xi_k \equiv \sup_{t \geq 0} |\eta_k(t)| < \infty$ a.s. for each k , and $E[e^{\alpha \xi_k}] < \infty$ for each k , for some $\alpha > 0$. Define $l(t) \equiv \log(t) \vee \sqrt{2}$. Then $N_k(t) = t + W_k(t) + l(t)\eta_k(t)$, $t \geq 0$.

Back to the $\bar{X}^r(t)$ equation:

$$\begin{aligned} \bar{X}^r(t) &= \bar{X}^r(0) + \sum_{k=1}^K \frac{1}{r} \left(\int_0^t r f_k^r(\bar{X}^r(s)) ds \right) (\nu'_k - \nu_k) \\ &\quad + \sum_{k=1}^K \frac{1}{r} W_k \left(r \int_0^t f_k^r(\bar{X}^r(s)) ds \right) (\nu'_k - \nu_k) \\ &\quad + \sum_{k=1}^K \frac{1}{r} l \left(r \int_0^t f_k^r(\bar{X}^r(s)) ds \right) \eta_k \left(r \int_0^t f_k^r(\bar{X}^r(s)) ds \right) (\nu'_k - \nu_k). \end{aligned}$$

7 “Mass” of Network

A diagram was drawn of a continuous flow stirred tank reactor with a conservative reaction system inside and with additional inflows and outflows. Inflow reactions are of the form $\emptyset \rightarrow A_i$ and outflow reactions are of the form $A_i \rightarrow \emptyset$.

Definition 1. (*Conserved quantity*) A vector $m \in \mathbb{R}_{>0}^n$ is a conserved quantity for reaction k if $m \cdot (\nu'_k - \nu_k) = 0$.

If m is conserved for all of the reactions, then $m \cdot \bar{X}^r(t) = m \cdot \bar{X}^r(0) \forall t \geq 0$.

Example:

$$A + B \rightarrow C, \quad S = \begin{pmatrix} -1 \\ -1 \\ 1 \end{pmatrix} = (\nu' - \nu)$$

then $m = (1, 1, 2)$ is a conserved quantity. At this point a picture was drawn of the simplex given by $\{x \in \mathbb{R}_{\geq 0}^3 : m \cdot x = d_0\}$ for some $d_0 > 0$, indicating a set in which the dynamics will constrain the stochastic process $\bar{X}^r$ when starting with a deterministic initial condition.

Suppose that a subset indexed by $k = 1, \dots, K_1$ of the reactions are conservative (i.e., there is $m \in \mathbb{R}_{>0}^n$ such that $m \cdot (\nu'_k - \nu_k) = 0$, $k = 1, \dots, K_1$), and the reactions indexed by $k = K_1 + 1, \dots, K_2$ for some $K_2 \geq K_1$, correspond to outflows (so that $\nu'_k - \nu_k = -\nu_k$ for these reactions) and the reactions indexed by $k = K_2 + 1, \dots, K$ correspond to inflows (so that $\nu_k = 0$ for these k).

Then,

$$m \cdot \bar{X}^r(t) \leq m \cdot \bar{X}^r(0) + \sum_{\substack{k=K_2+1 \\ \text{inflows}}}^K \frac{1}{r} N_k \left(r \int_0^t f_k^r(\bar{X}^r(s)) ds \right) \underbrace{m \cdot \nu'_k}_{d_k}$$

For an inflow reaction indexed by k , this reaction has the form $\emptyset \rightarrow A_i$ for some species A_i and $f_k^r(c) = \tilde{\kappa}_k$ (no concentrations involved). This yields a

major simplification of the above expression where we now also incorporate the strong approximation:

$$\begin{aligned}
m \cdot \bar{X}^r(t) &\leq m \cdot \bar{X}^r(0) + \sum_{k \geq K_2+1} \frac{d_k}{r} [rt\tilde{\kappa}_k + W_k(rt\tilde{\kappa}_k) + l(rt\tilde{\kappa}_k)\eta_k(rt\tilde{\kappa}_k)] \\
&\leq m \cdot \bar{X}^r(0) + \sum_{k \geq K_2+1} d_k t \tilde{\kappa}_k \\
&\quad + \sum_{k \geq K_2+1} d_k |\xi_k| \frac{\log(rt\tilde{\kappa}_k) \vee \sqrt{2}}{r} + \sum_{k \geq K_2+1} d_k \frac{W_k(rt\tilde{\kappa}_k)}{r}.
\end{aligned}$$

Note that by the ‘time is like distance squared scaling of Brownian motion’,

$$\frac{W_k(r\tilde{\kappa}_k \cdot)}{r} \stackrel{dist}{=} \sqrt{r} \frac{W_k(\tilde{\kappa}_k \cdot)}{r} \Rightarrow 0 \quad \text{as } r \rightarrow \infty.$$

It then follows from this and the inequality above that, with high probability, we can find a uniform bound on $m \cdot \bar{X}^r$ on the time interval $[0, T]$ for all r sufficiently large. That is, given $T > 0$ and $\epsilon > 0$, there is $K^* = K(\epsilon, T)$, $r^* = r(\epsilon, T)$ such that for all $r \geq r^*$,

$$P(\|m \cdot \bar{X}^r(\cdot)\|_T \geq K^*) < \epsilon.$$

Since $m > 0$, it follows from this that there is a suitable constant $\tilde{K}^*$ such that for all $r \geq r^*$,

$$P(\|\bar{X}^r(\cdot)\|_T \geq \tilde{K}^*) < \epsilon.$$

This gives us compact containment. We shall deal with oscillations next time.