

Biochemical Reaction Network Notes, Monday November 3, 2008

Notetaker: Michael Kinnally

Recall, $\{\bar{X}^r(t), t \geq 0\}$ represents the “concentration” process taking values in $\mathbb{R}_+^n$ for a chemical reaction system in a well-mixed tank of volume r . For each $k = 1, \dots, K$, $N_k(\cdot)$ is a unit rate Poisson process, $\tilde{\kappa}_k$ is the normalized rate constant of the k^{th} reaction $\nu_k \rightarrow \nu'_k$, and

$$f_k^r(c) := \tilde{\kappa}_k \prod_{i=1}^n c_i (c_i - \frac{1}{r}) \cdots (c_i - \frac{\nu_{ik} - 1}{r}), \quad c \in \mathbb{R}_{\geq 0}^n,$$

where there are ν_{ik} terms in the i^{th} term in the product. Then as was shown last time, $\bar{X}^r$ satisfies the following equation for all $t \geq 0$:

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

For each $k = 1, \dots, K$ and $r > 0$, define the rescaled processes

$$\bar{N}_k^r(\cdot) = \{\bar{N}_k^r(t) := \frac{N_k(rt)}{r}, t \geq 0\}.$$

Then,

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

For each $k = 1, \dots, K$, define the function

$$f_k(c) = \tilde{\kappa}_k \prod_{i=1}^n c_i^{\nu_{ik}} = \tilde{\kappa}_k c^{\nu_k}, \quad c \in \mathbb{R}_{\geq 0}^n.$$

Then for each $k = 1, \dots, K$, $f_k^r \rightarrow f_k$ uniformly on compact subsets of $\mathbb{R}_{\geq 0}^n$ as $r \rightarrow \infty$, and

$$\sup_r |f_k^r(\bar{X}^r(\cdot))| \leq f_k(\bar{X}^r(\cdot)).$$

Our Aim: To show $\{\bar{X}^r\}_{r>0}$ is C-tight and to characterize its weak limit points.

Recall the following criterion for C-tightness of a sequence $\{Y^r\}_{r=1}^\infty$ of processes with paths in $\mathbb{D}^n$.

C-Tightness Criterion. For each $T > 0, \varepsilon > 0$, there are $K^* = K(T, \varepsilon), r^* = r(T, \varepsilon), \delta^* = \delta(T, \varepsilon)$ such that

- (i) $P(\|Y^r(\cdot)\|_T \geq K^*) < \varepsilon$ for all $r \geq r^*$, and
- (ii) $P(w(Y^r, \delta^*, T) > \varepsilon) < \varepsilon$ for all $r \geq r^*$.

Last time, we showed the compact containment property for $\{\bar{X}^r\}$, i.e., (i) holds with $\{\bar{X}^r\}$ in place of $\{Y^r\}$. Thus, for each $T > 0, \varepsilon > 0$ there exists K^*, r^* such that if we define, for each $r > 0$, the set $G^{\varepsilon, r} := \{\|\bar{X}^r(\cdot)\|_T < K^*\}$ of “good outcomes”, then

$$P(G^{\varepsilon, r}) \geq 1 - \varepsilon \quad \text{for all } r \geq r^*.$$

Since $|f_k^r(\bar{X}^r(\cdot))| \leq f_k(\bar{X}^r(\cdot)) = \tilde{\kappa}_k \prod_{i=1}^n (\bar{X}_i^r(\cdot))^{\nu_{ik}}$, if we have an upper bound on $\bar{X}^r(\cdot)$, then we will have a bound on $f_k^r(\bar{X}^r(\cdot))$ that is uniform in r . Thus, for $r \geq r^*$, on $G^{\varepsilon, r}$ we have for all $s \in [0, T]$,

$$|f_k^r(\bar{X}^r(s))| \leq \sup_{k=1}^K \tilde{\kappa}_k \prod_{i=1}^n (K^*)^{\nu_{ik}} =: M^* = M(\varepsilon, T).$$

By the C-tightness criterion, and since $\bar{X}^r(0) \Rightarrow \bar{X}_0$, in order to prove C-tightness of $\{\bar{X}^r\}$, it suffices to prove that for each $k = 1, \dots, K$,

$$\left\{ \bar{N}_k^r \left(\int_0^t f_k^r(\bar{X}^r(s)) ds \right), t \geq 0 \right\}_{r>0}$$

is C-tight.

Exercise: Prove the sufficiency for yourself.

From the functional central limit theorem for renewal processes, we have

$$(\bar{N}_1^r(\cdot), \dots, \bar{N}_K^r(\cdot)) \Rightarrow (e(\cdot), \dots, e(\cdot)),$$

where $e(\cdot)$ is the deterministic process: $e(t) = t, t \geq 0$. This also follows from the strong approximation result. Recall that $N_k(t) = t + W_k(t) + (2 \vee \log(t))\eta_k(t)$, where $\exp(\alpha \|\eta_k\|_{[0, \infty)})$ has finite expectation for some $\alpha > 0$. Then

$$\begin{aligned} \bar{N}_k^r(t) &= \frac{\bar{N}_k(rt)}{r} \\ &= t + \frac{W_k(rt)}{r} + \frac{(2 \vee \log(rt))\eta_k(rt)}{r} \\ &\stackrel{d}{=} t + \frac{\tilde{W}_k(t)}{\sqrt{r}} + \frac{(2 \vee \log(rt))\eta_k(rt)}{r}, \end{aligned} \tag{1}$$

where $\tilde{W}_k(\cdot) := \frac{W(r\cdot)}{\sqrt{r}}$ is a Brownian motion due to Brownian scaling, and thus the right-hand side of (1) tends to the process $e(\cdot)$ in distribution as $r \rightarrow \infty$.

Define for each $k = 1, \dots, K$,

$$\bar{\Phi}_k^r(t) := \int_0^t f_k^r(\bar{X}^r(s)) ds, \quad t \geq 0,$$

so that $\bar{\Phi}_k^r \in \mathbb{D}_0$ (the set of “time changes”).

Lemma 1. *The set $\{\bar{\Phi}_k^r\}_{r>0}$ of processes is C-tight for each k .*

Proof. (i) $P(\|\bar{\Phi}_k^r\|_T \leq M^*T) \geq P(G^{\varepsilon,r}) \geq 1 - \varepsilon$ for all $r \geq r^*$.

(ii) For $r \geq r^*$, on $G^{\varepsilon,r}$:

$w(\bar{\Phi}_k^r, \delta, T) \leq M^*\delta \leq \varepsilon$ if $\delta \leq \frac{\varepsilon}{M^*}$. So $w(\bar{\Phi}_k^r, \frac{\varepsilon}{M^*}, T) \leq \varepsilon$. Therefore,

$$P\left(w(\bar{\Phi}_k^r, \frac{\varepsilon}{M^*}, T) \leq \varepsilon\right) \geq P(G^{\varepsilon,r}) \geq 1 - \varepsilon.$$

□

Since $\{(\bar{N}_1^r, \dots, \bar{N}_K^r)\}_{r>0}$ converges to a continuous process, it is automatically C-tight. Combining this with Lemma 1, we get that

$$\{(\bar{N}_1^r, \dots, \bar{N}_K^r, \bar{\Phi}_1^r, \dots, \bar{\Phi}_K^r)\}_{r>0} \text{ is C-tight.}$$

Lemma 2. *$\{(\bar{N}_1^r(\bar{\Phi}_1^r(\cdot)), \dots, \bar{N}_K^r(\bar{\Phi}_K^r(\cdot)))\}_{r>0}$ is C-tight.*

Proof. It suffices to show that $\{\bar{N}_k^r(\bar{\Phi}_k^r(\cdot))\}_{r>0}$ is C-tight for each $k = 1, \dots, K$. Recall that

C-tightness $\Leftrightarrow$ tightness and each weak limit point is continuous.

Take a subsequence indexed by $\{r_\ell\}_{\ell=1}^\infty$. Since $\{(\bar{N}_1^{r_\ell}, \dots, \bar{N}_K^{r_\ell}, \bar{\Phi}_1^{r_\ell}, \dots, \bar{\Phi}_K^{r_\ell})\}_{\ell=1}^\infty$ is C-tight, it has a subsequence indexed by $\{r_{\ell_m}\}_{m=1}^\infty$ say, that converges weakly to a continuous process. In particular, $\{(\bar{N}_k^{r_{\ell_m}}, \bar{\Phi}_k^{r_{\ell_m}})\}_{m=1}^\infty$ converges weakly to some continuous process $(\bar{N}_k, \bar{\Phi}_k)$. Therefore, by the random time-change theorem, $\{\bar{N}_k^{r_{\ell_m}}(\bar{\Phi}_k^{r_{\ell_m}}(\cdot))\}_{m=1}^\infty$ converges weakly to $\bar{N}_k(\bar{\Phi}_k(\cdot))$, which is continuous.

□

It follows that since for each $t \geq 0$,

$$\bar{X}^r(t) = \bar{X}^r(0) + \sum_{k=1}^K \bar{N}_k^r(\bar{\Phi}_k^r(t))(\nu'_k - \nu_k), \quad (2)$$

then by Lemma 2, and since $\overline{X}^r(0) \Rightarrow \overline{X}_0$, we have that

$$\{\overline{X}^r\}_{r>0} \text{ is C-tight.}$$

Suppose $\overline{X}$ is a weak limit point of $\{\overline{X}^r\}$. By choosing a suitable subsequence which we again index by r , we can assume that $\{(\overline{X}^r, \overline{N}_1^r, \dots, \overline{N}_K^r, \overline{\Phi}_1^r, \dots, \overline{\Phi}_K^r)\}$ converges weakly to a continuous process $(\overline{X}, e, \dots, e, \overline{\Phi}_1, \dots, \overline{\Phi}_K)$. By Skorokhod's representation theorem, without loss of generality we can assume that the convergence is a.s. uniformly on compact time intervals, and that (*) holds for each r .

Fix $t \geq 0$ and pass to the limit as $r \rightarrow \infty$ in (2). Since a.s., $\overline{X}^r \rightarrow \overline{X}$ uniformly on $[0, t]$, and $f_k^r \rightarrow f_k$ uniformly on compact sets for each k , it follows that a.s.,

$$f_k^r(\overline{X}^r(\cdot)) \rightarrow f_k(\overline{X}(\cdot)) \text{ uniformly on } [0, t] \text{ as } r \rightarrow \infty.$$

Hence a.s., as $r \rightarrow \infty$,

$$\overline{\Phi}_k^r(t) = \int_0^t f_k^r(\overline{X}^r(s)) ds \rightarrow \overline{\Phi}_k(t) = \int_0^t f_k(\overline{X}(s)) ds.$$

Combining this with the convergence of $\overline{N}_k^r$ to e uniformly on compact time intervals, we obtain that

$$\overline{N}_k^r(\overline{\Phi}_k^r(t)) \rightarrow \overline{\Phi}_k(t) \text{ a.s., as } r \rightarrow \infty.$$

Letting $r \rightarrow \infty$ in (2), we obtain that a.s.,

$$\overline{X}(t) = \overline{X}(0) + \sum_{k=1}^K \left(\int_0^t f_k(\overline{X}(s)) ds \right) (\nu'_k - \nu_k), \quad t \geq 0.$$

Therefore, by the definition of f_k ,

$$\dot{\overline{X}}(t) = \frac{d}{dt} \overline{X}(t) = \sum_{k=1}^K \tilde{\kappa}_k \overline{X}(t)^{\nu_k} (\nu'_k - \nu_k),$$

or, in chemistry form (with c as the concentration vector),

$$\dot{c}(t) = \sum_{k=1}^K \tilde{\kappa}_k \prod_{i=1}^n c_i^{\nu_{ik}} (\nu'_k - \nu_k), \quad c \in \mathbb{R}_{\geq 0}^n \quad (3)$$

If we set $r_k(c) := \tilde{\kappa}_k c^{\nu_k}$ for each $k = 1, \dots, K$, then this reduces to

$$\dot{c}(t) = Sr(c),$$

where S is the stoichiometric matrix, which has $(\nu'_k - \nu_k)$ as its k^{th} column.

Since the coefficients of (3) are locally Lipschitz continuous, we get local uniqueness. To get global uniqueness, we just need to show that the solutions do not explode in finite time.

Recall, for a mass vector $m \in \mathbb{R}_{>0}^n$,

$$m \cdot \dot{c} \leq \sum_{\substack{\text{inflows} \\ k}} \tilde{\kappa}_k m \cdot \nu'_k,$$

and this last term is a finite constant, L . Then we'll have the bound $\frac{d}{dt}(m \cdot c(t)) \leq L$, and since $m \in \mathbb{R}_{>0}$, the solution cannot explode in finite time.

Since $\{\overline{X}^r\}_{r \geq 0}$ is C-tight and we have uniqueness in law of weak limit points, it follows that $\{\overline{X}^r\}$ converges in distribution to a continuous process $\overline{X}$ that is a.s. the unique solution to

$$\overline{X}(t) = \overline{X}(0) + \sum_{k=1}^K \left(\int_0^t f_k(\overline{X}(s)) ds \right) (\nu'_k - \nu_k), \quad t \geq 0.$$

This unique solution $\overline{X}$ is sometimes called the continuum limit, or the large-volume limit.