Circulation theory of enzyme kinetics

Yuhao Jiang

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Here we adopt the presentation given by Kalpazatidou. Let $(\xi_l)_{l\geq 0}$ be a discrete-time Markov chain with finite state space S defined on some space $(\Omega, \mathcal{F}, P)$.

Definition 0.1. A circuit function in a finite set S is a periodic function c, which maps the set **Z** of integers to S.

Definition 0.2. Let $\mathcal{C}_n(\omega)$ be the class of cycles occurring along the sample path $(\xi_l)_{l\geq 0}$ until time n. Then we use $\mathcal{C}_\infty$ to represent the limit of $\mathcal{C}_n$ as $n \to \infty$. This convergence has been proofed in [].

Definition 0.3. Let N_n^c denote the number of time that cycle c is formed by a Markov chain up to time n. Then the sample circulation J_n^c along cycle c by time t is defined as

$$J_n^c = \frac{1}{n} N_n^c$$

and the circulation J^c along cycle c is a nonnegative real number defined as the following almost sure limit:

$$J^c = \lim_{n\to\infty} J_n^c, \quad a.s.$$

which represents the number of times that cycle c ic formed per unit time.

Definition 0.4. Let $\{\mu_n : n \in N^*\}$ be a family of probability measures on a Polish space E. Then we say that $\{\mu_n : n \in N^*\}$ satisfies a large deviation principle with rate n and good rate function $I : E \to [0, \infty]$ if:

(i) for each $\alpha > 0$, the level set $\{x \in E : I(x) < \alpha\}$ is compact in E;

(ii) for each closed subset F of E,

$$\limsup_{n\to\infty} \frac{1}{n} \log \mu_n(F) \leq -\inf_{x\in F} I(x); \tag{1}$$

(iii) for each open subset U of E,

$$\liminf_{n\to\infty} \frac{1}{n} \log \mu_n(U) \geq -\inf_{x\in U} I(x); \tag{2}$$

1 Large deviation of circulation for finite Markov chains

We consider the following n-step($n \geq 2$) enzyme kinetics model:

$$E + S \rightleftharpoons ES \rightleftharpoons EP_1 \rightleftharpoons EP_2 \rightleftharpoons \cdots EP_{n-2} \rightleftharpoons E + P$$

where E is an enzyme turning the substrate S into the product P. From the perspective of a single enzyme molecule, this enzyme kinetics can be modeled as n-step Markov chain $(\xi_l)_{l\geq 0}$, with finite state space S defined on some space $(\Omega, \mathcal{F}, P)$. If $n = 2$, then this Markov chain only have two state E and ES.

Theorem 1.1.

1.1 Large deviation of circulation for two state Markov chains

$$I(\nu) = \nu_1 \log(\frac{\nu_1}{\nu_1 + \nu_{12}}/\frac{w_1}{w_1 + w_{12}}) + \nu_2 \log(\frac{w_2}{w_1 + w_{12}}) + 2\nu_{12} \log(\frac{\nu_{12}}{\nu_1 + \nu_{12}}/\frac{w_{12}}{w_1 + w_{12}})$$

1.2 Large deviation of circulation for three state Markov chains

$$\begin{aligned}
I(\nu) = \sum_{i\in I} &\left(-\nu^i \log\frac{\nu^i}{w^i} + (\nu^i - \nu_i)\log(\nu^i - \nu_i)\right) \\
&- (\tilde{\nu} - \sum_{i\in I}\nu_i)\log(\tilde{\nu} - \sum_{i\in I}\nu_i) + \sum_{t\in C_\infty}\nu_t \log\nu_t \\
&- (\nu_1 \log w_1 + \nu_2 \log w_2 + \nu_3 \log w_3) \\
&- (\nu_{12} + \nu_{123})\log(w_{12} + w_{123}) \\
&- (\nu_{13} + \nu_{132})\log(w_{13} + w_{132}) \\
&- (\nu_{12} + \nu_{132})\log(w_{12} + w_{132}) \\
&- (\nu_{23} + \nu_{123})\log(w_{23} + w_{123}) \\
&- (\nu_{13} + \nu_{123})\log(w_{13} + w_{123}) \\
&- (\nu_{23} + \nu_{132})\log(w_{23} + w_{132})
\end{aligned}$$

where $I = \{1, 2, 3\}$ is the state space for Markov chains

$$\mathcal{C}_\infty = \{(1), (2), (3), (1,2), (2,3), (1,3), (1,2,3), (1,3,2)\}$$

is the class of all cycles occurring. ν_c is the frequence of c occurring, w_c is the circulation of c.
And $\nu^i = \sum_{J_{c_s}(i)=1}\nu_{c_s}$, such as $\nu^1 = \nu_1 + \nu_{12} + \nu_{13} + \nu_{123} + \nu_{132}$ $\tilde{\nu} = \nu_1 + \nu_2 + \nu_3 + \nu_{12} + \nu_{13} + \nu_{23} + \nu_{123} + \nu_{132}$
w^i, w_i has the similar definition.

1.3 Large deviation of circulation for multi-state Markov chains