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ASYMPTOTIC ANALYSIS FOR STATIONARY DISTRIBUTIONS OF MULTISCALED REACTION NETWORKS

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Abstract

We study stationary distributions in the context of stochastic reaction networks. In particular, we are interested in complex balanced reaction networks and the reduction of such networks by assuming that a set of species (called non-interacting species) are degraded fast (and therefore essentially absent from the network), implying that some reaction rates are large relative to others. Technically, we assume that these reaction rates are scaled by a common parameter N and let $N \to \infty$. The limiting stationary distribution as $N \to \infty$ is compared with the stationary distribution of the reduced reaction network obtained by elimination of the non-interacting species. In general, the limiting stationary distribution could differ from the stationary distribution of the reduced reaction network. We identify various sufficient conditions under which these two distributions are the same, including when the reaction network is detailed balanced and when the set of non-interacting species consists of intermediate species. In the latter case, the limiting stationary distribution essentially retains the form of the complex balanced distribution. This finding is particularly surprising given that the reduced reaction network could be non-weakly reversible and might exhibit unconventional kinetics.

Keywords: Continuous-time Markov chain; stationary distribution; complex balanced; non-interacting species; multiscale system

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1. Introduction

Reaction networks are used to model the complex behaviour of chemical systems [3, 10]. Ordinary differential equations can be used to describe the evolution of species concentrations when the molecule counts in the system are relatively large. However, when the molecule counts are low, random fluctuations become significant, and probabilistic techniques need to

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be employed [22]. In such situations, continuous-time Markov chains (CTMCs) are commonly used to model the stochastic dynamics of the molecule counts. We refer readers to the monograph by Anderson and Kurtz [3] for an introduction to stochastic reaction networks, as well as to [20, 22] for early seminal work.

A first objective in the study of stochastic reaction networks is to investigate the stationary distributions of the CTMC, which describe the long-term behaviour of the system [1, 2, 8, 15, 16, 17]. In the present paper, we explore conditional and asymptotic properties of stationary distributions of multiscaled stochastic reaction networks. Multiscaled stochastic reaction networks are of relatively recent interest [7, 13, 19, 25] and build further on the seminal work of Kurtz [20], which revealed a correspondence over finite time intervals between a sequence of stochastic reaction networks with (parameter) scaled kinetics and a (limiting) deterministic reaction network. In contrast, little work has been done to characterise the limiting stationary distribution in a multiscale setting [8, 13]. We address this problem here; in particular, we focus on complex balanced stochastic reaction networks with *non-interacting species* (to be defined later), assuming a sequence of one-parameter scaled stochastic reaction networks. We consider the limiting stationary distribution of this family of reaction networks and compare it with the stationary distribution of the reaction network obtained by *elimination of non-interacting species* (to be defined later). In general, it is known that the limiting stationary distribution and the stationary distribution obtained by elimination of non-interacting species may not be the same; see [7, Example 5.4] and [13, Example 5.8].

To motivate our work, consider a reaction network with stochastic mass-action kinetics,

$$A \underset{2x_U}{\overset{x_A}{\rightleftharpoons}} U \underset{3x_B}{\overset{2x_U}{\rightleftharpoons}} B. \tag{1}$$

Here, A, B, and U represent distinct species, and x_A, x_B, and x_U are the molecule counts of the respective species. In addition, the edge labels are the intensity functions of the corresponding reactions. The intensity functions quantify the propensities of the reactions to occur.

The set $\Gamma = \{x_A + x_B + x_U = T\}$ for $T \in \mathbb{N}_0$ is an irreducible component of the CTMC. By a well-known result [2, Theorem 4.1], (1) has a unique Poisson-product-form stationary distribution on Γ given by

$$\pi(x_A, x_B, x_U) := M \frac{6^{x_A} 2^{x_B} 3^{x_U}}{x_A! x_B! x_U!}, \quad (x_A, x_B, x_U) \in \Gamma,$$

where M is a positive constant such that π is a probability distribution. By applying a scaling factor N to the reaction rates of $U \longrightarrow A$ and $U \longrightarrow B$, we obtain a one-parameter sequence of stochastic reaction networks with stationary distribution

$$\pi_N(x_A, x_B, x_U) := M_N \frac{6^{x_A} 2^{x_B} (3/N)^{x_U}}{x_A! x_B! x_U!} = M_N N^{-x_U} \frac{6^{x_A} 2^{x_B} 3^{x_U}}{x_A! x_B! x_U!}$$

for all $(x_A, x_B, x_U) \in \Gamma$ and $N \in \mathbb{N}$, where $M_N > 0$ is a constant depending on N. This can be illustrated with a line graph, using R and ggplot2 [26, 28], plotting the marginal probabilities for species U on Γ with $T = 5$; see Figure 1.

Letting $N \to \infty$, one finds that π_N converges pointwise to a probability distribution π_0 on Γ given by

$$\pi_0(x_A, x_B) := \begin{cases} \frac{1}{\pi(\Gamma_0)} \pi(x_A, x_B), & (x_A, x_B) \in \Gamma_0 := \{x_A + x_B = T\}, \\ 0, & \text{otherwise.} \end{cases}$$

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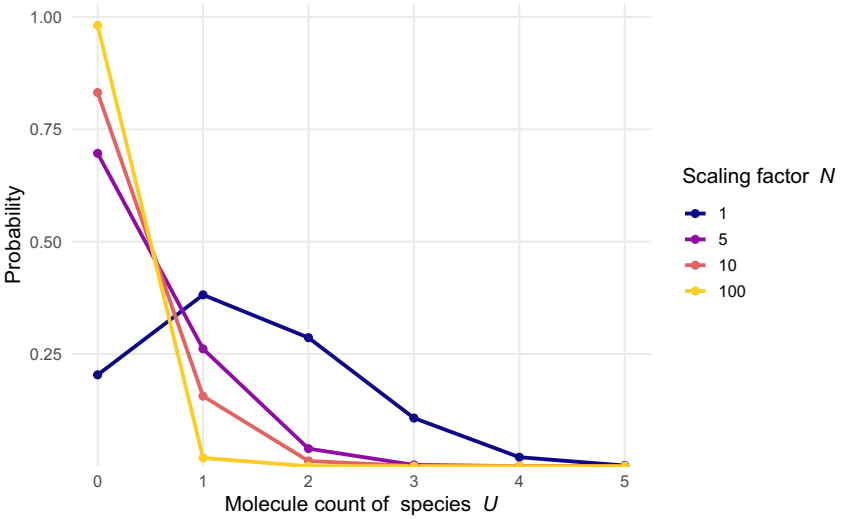

FIGURE 1. Marginal stationary distribution for the molecule count of species U on the irreducible component $\Gamma = \{x_A + x_B + x_U = T\}$ with $T = 5$, for different N.

This distribution π_0 is in fact the unique stationary distribution of the reaction network on Γ_0 with stochastic mass-action kinetics:

$$A \underset{3x_B/2}{\overset{x_A/2}{\rightleftharpoons}} B. \tag{2}$$

Moreover, the reaction network (2) can be seen as a reduced stochastic reaction network by elimination of the species U, in the sense of [13, 14].

This motivating example raises the natural question of how general these observations are. We will address this question in the context of weakly reversible reaction networks with a complex balanced distribution and a set of non-interacting species. The species U in the example is a non-interacting species.

In this context, we will show that the conditional distribution is a stationary distribution of a reduced stochastic reaction network obtained by elimination of the non-interacting species [13, 14]; cf. (2). Furthermore, this reduced reaction network could be considered the natural limit of a one-parameter sequence of scaled reaction networks, as in the example. Most proofs are given in a separate section at the end of the paper.

The concepts of non-interacting species and reduced reaction networks were introduced in [11] within the framework of variable elimination for deterministic reaction networks, building on the notion of intermediate species [12]. These concepts are widely applicable to realistic models of chemical reaction networks [21]. Non-interacting species are typically considered physically short-lived molecules. In the stochastic setting, convergence of CTMCs over finite time intervals has been studied for intermediate species as well as non-interacting species in a multiscale framework by means of the reduced reaction network [7, 13]. Here, we identify sufficient conditions for this correspondence to hold at $t = \infty$.

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2. Preliminaries

2.1. Notation

Let $\mathbb{R}$, $\mathbb{R}_{\geq 0}$, and $\mathbb{R}_{>0}$ be the sets of real, non-negative, and positive numbers, respectively. Let $\mathbb{N}$ and $\mathbb{N}_0$ be the sets of positive and non-negative integers, respectively, and let $\mathbb{Z}$ denote the set of integers. For $x = (x_1, \dots, x_n) \in \mathbb{R}^n$ and $y = (y_1, \dots, y_n) \in \mathbb{R}^n$, we say that $x \geq y$ if $x_i \geq y_i$ for all $i = 1, \dots, n$ and that $x > y$ if $x \geq y$ and $x \neq y$. In addition, we define $x \vee y = (\max\{x_1, y_1\}, \dots, \max\{x_n, y_n\})$ and $\langle x, y\rangle = \sum_{i=1}^n x_i y_i$ for the inner product on $\mathbb{R}^n$. For a finite set $\mathcal{I}$, $|\mathcal{I}|$ denotes the cardinality of $\mathcal{I}$.

2.2. Reaction networks

A *reaction network* is a triple $\mathcal{N} = (\mathcal{S}, \mathcal{C}, \mathcal{R})$ of three finite sets: a set $\mathcal{S} = \{S_1, \dots, S_n\}$ of *species*, a set $\mathcal{C}$ of *complexes*, which are non-negative linear combinations of the species (complexes are identified as elements of $\mathbb{N}_0^n$), and a set $\mathcal{R}$ of *reactions*, which are elements of $\mathcal{C} \times \mathcal{C}$. One could regard $(\mathcal{C}, \mathcal{R})$ as a digraph. We assume that all species have a positive coefficient in some complex and that every complex is the source or target of some reaction. In this case, $\mathcal{C}$ and $\mathcal{S}$ can be determined from $\mathcal{R}$. In examples, we simply draw the reactions.

For simplicity, for a reaction $r \in \mathcal{R}$, we write $r = (y, y')$ or $r = y \longrightarrow y'$, where y is the source of r and y' the target. In the chemical literature, these are called the *reactant* $\mathrm{reac}(r) = y$ and the *product* $\mathrm{prod}(r) = y'$ of r, respectively. The *reaction vector* of r is $\zeta(r) = y' - y \in \mathbb{Z}^n$.

We introduce an associative binary operation [14]

$$\begin{aligned} \oplus : \left(\mathbb{N}_0^n \times \mathbb{N}_0^n\right) \times \left(\mathbb{N}_0^n \times \mathbb{N}_0^n\right) &\to \mathbb{N}_0^n \times \mathbb{N}_0^n, \\ (y_1, y_1') \oplus (y_2, y_2') &:= \left(y_1 + 0 \vee (y_2 - y_1'),\ y_2' + 0 \vee (y_1' - y_2)\right) \end{aligned} \tag{3}$$

for $(y_1, y_1'), (y_2, y_2') \in \mathbb{N}_0^n \times \mathbb{N}_0^n$. It can be interpreted as the sum of two reactions; for example,

$$\big((1,1,0),(0,0,1)\big) \oplus \big((0,1,1),(0,1,0)\big) = \big((1,2,0),(0,1,0)\big)$$

corresponds to the sum (cf. [18, Subsection 3.1.2])

$$S_1 + S_2 \longrightarrow S_3 \quad \oplus \quad S_2 + S_3 \longrightarrow S_2 \quad = \quad S_1 + 2S_2 \longrightarrow S_2.$$

The left-hand side of the sum consists of the molecules required for the two reactions to proceed in succession, and the right-hand side consists of the molecules that are produced and not consumed in the two reactions.

In the following, we assume that a reaction network $\mathcal{N} = (\mathcal{S}, \mathcal{C}, \mathcal{R})$ is given.

Definition 1. *A state $x_1 \in \mathbb{N}_0^n$ leads to $x_2 \in \mathbb{N}_0^n$ via $\mathcal{N}$, denoted by $x_1 \to_{\mathcal{N}} x_2$, if there exists reactions $r_1, \dots, r_k \in \mathcal{R}$ such that $r_1 \oplus \cdots \oplus r_k = (y, y')$ with $x_1 \geq y$ and $x_2 - x_1 = y' - y$.*

Definition 2. ([8, Definition 10].) *A set $\Gamma \subseteq \mathbb{N}_0^n$ is an irreducible component of $\mathcal{N}$ if for all $x \in \Gamma$ and all $z \in \mathbb{N}_0^n$, $x \to_{\mathcal{N}} z$ if and only if $z \in \Gamma$.*

Definition 3. ([10, Definitions 6.5.1 and 6.5.3].) *A reaction network is:*

(i) *reversible if $y \longrightarrow y' \in \mathcal{R}$ implies $y' \longrightarrow y \in \mathcal{R}$;*

(ii) *weakly reversible if for any $y \longrightarrow y' \in \mathcal{R}$, there exists a sequence $r_1, \dots, r_m \in \mathcal{R}$ satisfying $\mathrm{reac}(r_1) = y'$, $\mathrm{prod}(r_i) = \mathrm{reac}(r_{i+1})$ for all $i = 1, \dots, m-1$, and $\mathrm{prod}(r_m) = y$.*

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In graph terminology, a reaction network is weakly reversible if the components of the digraph $(\mathcal{C}, \mathcal{R})$ are strongly connected.

A *stochastic reaction network* (SRN) models the stochastic dynamics of a reaction network. Specifically, the evolution of the molecule counts, $(X(t) : t \in \mathbb{R}_{\geq 0})$, is modelled as an $\mathbb{N}_0^n$-valued CTMC satisfying the following stochastic equation:

$$X(t) = X(0) + \sum_{r \in \mathcal{R}} Y_r\left(\int_0^t \lambda_r(X(s))\, \mathrm{d}s \right) \zeta(r), \tag{4}$$

where $(Y_r : r \in \mathcal{R})$ is a collection of independent and identically distributed unit-rate Poisson processes and $\lambda = (\lambda_r : r \in \mathcal{R})$ is a collection of non-negative intensity functions on $\mathbb{N}_0^n$, known as the *kinetics*. *Stochastic mass-action kinetics* is commonly assumed in the literature; however, it is not a prerequisite for the majority of this paper's content. For a reaction $r = y_r \to y_r'$, the intensity function under mass-action kinetics takes the form

$$\lambda_r(x) = \kappa_r \frac{x!}{(x - y_r)!} = \kappa_r \prod_{i=1}^{n} \frac{x_i!}{(x_i - y_{r,i})!}$$

for some positive constant κ_r.

An SRN is denoted by $(\mathcal{N}, \lambda)$. Throughout, we assume the following compatibility condition.

Condition 1. *For any $r = y \longrightarrow y' \in \mathcal{R}$, $\lambda_r(x) > 0$ if and only if $x \geq y$.*

If Condition 1 is fulfilled, then $x \to_{\mathcal{N}} z$ implies that there is positive probability of going from x to z and vice versa.

A probability measure π on an irreducible component $\Gamma \subseteq \mathbb{N}_0^n$ of $(\mathcal{N}, \lambda)$ is (see [5, Definition 4.1]):

(i) a *stationary distribution* if for all $x \in \Gamma$,

$$\pi(x) \sum_{r \in \mathcal{R}} \lambda_r(x) = \sum_{r \in \mathcal{R}} \pi\big(x - \zeta(r)\big) \lambda_r\big(x - \zeta(r)\big); \tag{5}$$

(ii) a *complex balanced distribution* if for all complexes $\eta \in \mathcal{C}$ and all $x \in \Gamma$,

$$\pi(x) \sum_{y' :\, \eta \to y' \in \mathcal{R}} \lambda_{\eta \to y'}(x) = \sum_{y :\, y \to \eta \in \mathcal{R}} \pi(x + y - \eta) \lambda_{y \to \eta}(x + y - \eta); \tag{6}$$

(iii) a *detailed balanced distribution* if $\mathcal{N}$ is reversible and for all $y \longrightarrow y' \in \mathcal{R}$,

$$\pi(x) \lambda_{y \to y'}(x) = \pi(x + y' - y) \lambda_{y' \to y}(x + y' - y).$$

We reserve the term 'stationary distribution' for a distribution on a single irreducible component. Hence, a stationary distribution π on an irreducible component Γ of $(\mathcal{N}, \lambda)$ satisfies $\pi(x) > 0$ for all $x \in \Gamma$. Equation (5) is known in the chemical literature as the *master equation* (also the *Kolmogorov forward equation*) for the SRN $(\mathcal{N}, \lambda)$; see [3]. A detailed balanced distribution is a complex balanced distribution, and a complex balanced distribution is a stationary distribution.

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2.3. Non-interacting species and reduction

Let $\mathcal{N} = (\mathcal{C}, \mathcal{R}, \mathcal{S})$ be a reaction network, and let $\mathcal{U} = \{U_1, \dots, U_m\}$ be a proper subset of $\mathcal{S}$. Order the species such that

$$\mathcal{S} \setminus \mathcal{U} = \{S_1, \dots, S_{n-m}\} \quad \text{and} \quad \mathcal{S} = \{S_1, \dots, S_{n-m}, U_1, \dots, U_m\}.$$

Let $x = (z, u) \in \mathbb{N}_0^{n-m} \times \mathbb{N}_0^m = \mathbb{N}_0^n$ with $z = (z_1, \dots, z_{n-m})$ and $u = (u_1, \dots, u_m)$. We define the projection $\rho : \mathbb{N}_0^n \to \mathbb{N}_0^m$ onto the space of the species in $\mathcal{U}$ by

$$\rho(x) = \sum_{i=1}^{m} u_i U_i \in \mathbb{N}_0^m \quad \text{for } x = (z, u) \in \mathbb{N}_0^n. \tag{7}$$

Definition 4. ([11, Definition 6.1].) *The set $\mathcal{U}$ is a set of non-interacting species if for any $y \in \mathcal{C}$, either $\rho(y) = 0$ or $\rho(y) = U_i$ for some $U_i \in \mathcal{U}$. The complement $\mathcal{S} \setminus \mathcal{U}$ is the set of core species.*

Example 1. *Consider the reaction network (see [18, Subsection 3.1.2])*

$$E + A \rightleftharpoons EA, \quad EA + B \rightleftharpoons EAB, \quad EAB \longrightarrow E + P + Q. \tag{8}$$

It models the conversion of two substrates A and B into two other substrates P and Q by means of an enzyme E and several short-lived intermediate molecules, EA and EAB. Therefore, it is natural to treat $\mathcal{U} = \{EA, EAB\}$ as a set of non-interacting species, and thus $\mathcal{S} \setminus \mathcal{U} = \{E, A, P, Q\}$ is a set of core species. The choice is not unique; for example, $\mathcal{U} = \{E, EA, EAB\}$ is also a set of non-interacting species.

For a set $\mathcal{U} = \{U_1, U_2, \dots, U_m\}$ of non-interacting species, let $\{\mathcal{C}_0, \mathcal{C}_1, \dots, \mathcal{C}_m\}$ be the partition of $\mathcal{C}$ by

$$\mathcal{C}_i := \begin{cases} \{y \in \mathcal{C} : \rho(y) = 0\}, & i = 0, \\ \{y \in \mathcal{C} : \rho(y) = U_i\}, & 1 \le i \le m, \end{cases}$$

and let $\{\mathcal{R}_{i,j} : i, j = 0, \dots, m\}$ be the partition of $\mathcal{R}$ where

$$\mathcal{R}_{i,j} := \{y \longrightarrow y' : y \in \mathcal{C}_i,\ y' \in \mathcal{C}_j\}, \quad i, j = 0, \dots, m.$$

For the reaction network in (8) with $\mathcal{U} = \{EA, EAB\}$,

$$\begin{gathered} \mathcal{C}_0 = \{E + A, E + P + Q\}, \quad \mathcal{C}_1 = \{EA, EA + B\}, \quad \mathcal{C}_2 = \{EAB\}, \\ \mathcal{R}_{0,0} = \mathcal{R}_{0,2} = \mathcal{R}_{1,1} = \mathcal{R}_{2,2} = \varnothing, \quad \mathcal{R}_{0,1} = \{E + A \longrightarrow EA\}, \\ \mathcal{R}_{1,0} = \{EA \longrightarrow E + A\}, \quad \mathcal{R}_{1,2} = \{EA + B \longrightarrow EAB\}, \\ \mathcal{R}_{2,0} = \{EAB \longrightarrow E + P + Q\}, \quad \mathcal{R}_{2,1} = \{EAB \longrightarrow EA + B\}. \end{gathered}$$

We introduce a *multi-digraph* $(\mathcal{V}, \mathcal{E})$ (see [27]) with

$$\mathcal{V} = \{U_0\} \cup \mathcal{U} \quad \text{and} \quad \mathcal{E} = \{U_i \xrightarrow{r} U_j : r \in \mathcal{R}_{i,j},\ i, j = 0, \dots, m\},$$

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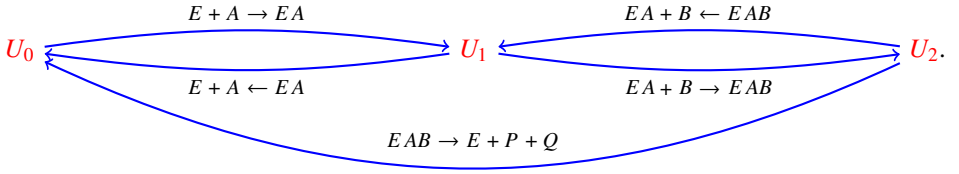
where U_0 is an additional node corresponding to all complexes not containing species in $\mathcal{U}$. There is a one-to-one correspondence between the edges $U_i \xrightarrow{r} U_j$ and the reactions $r \in \mathcal{R}_{i,j}$. As an example, the multi-digraph associated with (8) is



A q-step *walk* θ in $(\mathcal{V}, \mathcal{E})$ is a sequence of $q \in \mathbb{N}$ edges

$$\theta = U_{i_0} \xrightarrow{r_1} U_{i_1} \xrightarrow{r_2} \cdots \xrightarrow{r_q} U_{i_q},$$

where $r_k \in \mathcal{R}_{i_{k-1},i_k}$. A q-step walk is *closed* if $U_{i_0} = U_{i_q}$. If $U_{i_0} = U_0$, then U_{i_q} is said to be *produced*; and if $U_{i_q} = U_0$, then U_{i_0} is said to be *degraded*. Let $\mathcal{U}_{\text{pro}}$ and $\mathcal{U}_{\text{deg}}$ be the sets of produced and degraded non-interacting species, respectively.

For $q \in \mathbb{N}_0$ and $i \in \{0, \ldots, m\}$, we let $\Xi_i(q)$ be the collection of all $(q+1)$-step closed walks that start and end at U_i without passing though U_0. Then every element in $\Xi_i(q)$ is of the form

$$\gamma = U_i \xrightarrow{r_0} U_{i_1} \xrightarrow{r_1} \cdots \xrightarrow{r_{q-1}} U_{i_q} \xrightarrow{r_q} U_i, \tag{9}$$

where $i_1, \ldots, i_q \in \{1, \ldots, m\}$, $r_j \in \mathcal{R}_{i_j,i_{j+1}}$ for $0 \le j \le q$, and by definition $i_0 = i_{q+1} = i$. In particular, if $\gamma \in \Xi_i(0)$, then γ consists of one edge $U_i \xrightarrow{r} U_i$ only; and if $i = 0$, then γ is a reaction in $\mathcal{R}$ between core species only. Furthermore, define

$$\Xi_i := \bigcup_{q=0}^{\infty} \Xi_i(q), \quad i = 0, \ldots, m.$$

For the reaction network in (8) with $\mathcal{U} = \{EA, EAB\}$, we find that

$$\Xi_1(0) = \varnothing, \quad \Xi_1(1) = \left\{ U_1 \xrightarrow{EA+B \to EAB} U_2 \xrightarrow{EAB \to EA+B} U_1 \right\},$$

$$\Xi_1(2) = \varnothing, \quad \Xi_1(3) = \left\{ \begin{array}{l} U_1 \xrightarrow{EA+B \to EAB} U_2 \xrightarrow{EAB \to EA+B} U_1 \\ \qquad \xrightarrow{EA+B \to EAB} U_2 \xrightarrow{EAB \to EA+B} U_1 \end{array} \right\}.$$

Definition 5. ([12, Section 2].) *A set of non-interacting species $\mathcal{U}$ is a set of intermediate species if $y = \rho(y)$ for every $y \in \bigcup_{i=1}^{m} \mathcal{C}_i$.*

In (8), $\mathcal{U} = \{EA, EAB\}$ is a set of non-interacting species but not a set of intermediate species, because $EA + B \in \mathcal{C}_1$, yet $\rho(EA + B) = EA \neq EA + B$. On the other hand, if $\mathcal{U} = \{EAB\}$, then EAB is an intermediate species, since $\rho(EAB) = EAB$.

Definition 6. *Let $\mathcal{U}$ be a set of non-interacting species. If $\mathcal{U}_{\text{pro}} \subseteq \mathcal{U}_{\text{deg}}$, then $\mathcal{U}$ is said to be eliminable.*

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In (8) we have $\mathcal{U}_{\text{pro}} = \mathcal{U}_{\text{deg}}$, and thus $\mathcal{U}$ is eliminable. Definition 6 differs from Definition 4.1 of [14], with the latter encompassing more general situations. However, these two definitions align in the context of non-interacting species.

Lemma 1. *Let $\mathcal{N}$ be weakly reversible and $\mathcal{U}$ a set of non-interacting species. Then, $\mathcal{U}_{\text{pro}} = \mathcal{U}_{\text{deg}}$ and $\mathcal{U}$ is eliminable.*

Proof. To prove $\mathcal{U}_{\text{pro}} = \mathcal{U}_{\text{deg}}$, it suffices to prove the one-directional inclusion $\mathcal{U}_{\text{pro}} \subseteq \mathcal{U}_{\text{deg}}$. The reverse direction follows by the same reasoning. Let $U \in \mathcal{U}_{\text{pro}}$. Then there exists $q \in \mathbb{N}_{\geq 0}$ and a walk in $(\mathcal{V}, \mathcal{E})$,

$$U_0 \longrightarrow U_{i_1} \longrightarrow \cdots \longrightarrow U_{i_q} \longrightarrow U_i,$$

where the edge labels are skipped for simplification. If $q = 0$, then $U_0 \longrightarrow U_i \in \mathcal{E}$, and thus $U_i \in \mathcal{U}_{\text{deg}}$ by weak reversibility.

For $q \geq 1$, we prove the lemma by induction. First, $U_{i_q} \longrightarrow U_i$ implies the existence of a reaction $y \longrightarrow y' \in \mathcal{R}_{i_q,i}$. Then, owing to weak reversibility, there exists a sequence of reactions in $\mathcal{R}$ such that

$$y' \longrightarrow y_1 \longrightarrow \cdots \longrightarrow y_{q'} \longrightarrow y.$$

If there exists $j \in \{1, \ldots, q'\}$ such that $y_j \in \mathcal{C}_0$, then we are done. Otherwise, by the induction hypothesis, we have $U_{i_q} \in \mathcal{U}_{\text{deg}}$. This implies that there exists a walk of the form

$$U_0 \longrightarrow \cdots \longrightarrow U_{i_q} \longrightarrow U_i \longrightarrow \cdots \longrightarrow U_{i_q} \longrightarrow \cdots \longrightarrow U_0.$$

Therefore $U_i \in \mathcal{U}_{\text{deg}}$. The proof is complete. □

We introduce a map $\mathfrak{R}$ defined on the collection of all walks in $(\mathcal{V}, \mathcal{E})$:

$$\begin{aligned} \mathfrak{R}(\theta) &:= r_1 \oplus r_2 \oplus \cdots \oplus r_q \in \mathbb{N}_0^n \times \mathbb{N}_0^n, \\ \theta &= U_{i_1} \xrightarrow{r_1} U_{i_2} \xrightarrow{r_2} \cdots \xrightarrow{r_q} U_{i_{q+1}}. \end{aligned}$$

Then we have

$$\mathcal{R}_{i,i} = \mathfrak{R}(\Xi_i(0)) \subseteq \mathfrak{R}(\Xi_i), \quad i = 0, \ldots, m.$$

In particular, $\rho(y) = \rho(y') = 0$ for $\gamma \in \Xi_0$ with $\mathfrak{R}(\gamma) = (y, y')$.

Definition 7. *Let $\mathcal{U}$ be an eliminable set of species. The reduced reaction network $\mathcal{N}_{\mathcal{U}}$ obtained by elimination of $\mathcal{U}$ from $\mathcal{N}$ is a triple $(\mathcal{S}_{\mathcal{U}}, \mathcal{C}_{\mathcal{U}}, \mathcal{R}_{\mathcal{U}})$ where*

$$\mathcal{R}_{\mathcal{U}} := \mathfrak{R}(\Xi_0) \setminus \{(y, y) : y \in \mathbb{N}_0^{n_{\mathcal{U}}}\}, \quad \mathcal{C}_{\mathcal{U}} := \{y, y' : y \to y' \in \mathcal{R}_{\mathcal{U}}\},$$

$$\mathcal{S}_{\mathcal{U}} := \bigcup_{y \in \mathcal{C}_{\mathcal{U}}} \text{supp}(y) \subseteq \mathcal{S} \setminus \mathcal{U}.$$

Here, $\text{supp}(y) = \{S_i : y_i > 0\}$ *is the support of* $y = \sum_{j=1}^n y_j S_j$ *in* $\mathbb{N}_0^{\mathcal{S}}$, *and* $n_{\mathcal{U}} = |\mathcal{S}_{\mathcal{U}}|$.

By Definition 7, we find that for (8),

$$\mathfrak{R}(\Xi_0) = \left\{ \begin{matrix} E + A \longrightarrow E + A, \quad E + A + B \longrightarrow E + A + B, \\ E + A + B \longrightarrow E + P + Q \end{matrix} \right\},$$

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and thus the reduced reaction network is the triple $(\mathcal{S}_\mathcal{U}, \mathcal{C}_\mathcal{U}, \mathcal{R}_\mathcal{U})$ with

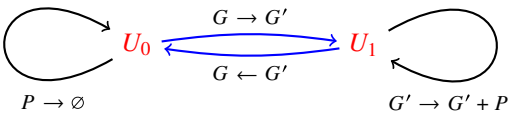
$$\mathcal{S}_\mathcal{U} = \{E, A, B, P, Q\}, \quad \mathcal{C}_\mathcal{U} = \{E + A + B, E + P + Q\}, \tag{10}$$
$$\mathcal{R}_\mathcal{U} = \{E + A + B \longrightarrow E + P + Q\}.$$

The set $\mathcal{R}_\mathcal{U}$ may contain infinitely many reactions, and thus the reduced reaction network may not be a reaction network.

Example 2. ([14, Example 2].) *Consider the following reaction network with* $\mathcal{U} = \{G'\}$*:*

$$G \rightleftharpoons G', \quad G' \longrightarrow G' + P, \quad P \longrightarrow \varnothing.$$

Then $\mathcal{C}_0 = \{P, \varnothing\}$, $\mathcal{C}_1 = \{G, G', G' + P\}$, $\mathcal{R}_{0,0} = \{P \longrightarrow \varnothing\}$, $\mathcal{R}_{0,1} = \{G \longrightarrow G'\}$, $\mathcal{R}_{1,0} = \{G' \longrightarrow G\}$, $\mathcal{R}_{1,1} = \{G' \longrightarrow G' + P\}$*, and the associated multi-digraph is*



Therefore, $\Xi_0(0) = \{U_0 \xrightarrow{\mathrm{P}} U_0\}$ *and*

$$\Xi_0(k) = \left\{U_0 \xrightarrow{G \to G'} \underbrace{U_1 \xrightarrow{G' \to G' + P} \cdots \xrightarrow{G' \to G' + P} U_1}_{k-1 \text{ steps}} \xrightarrow{G' \to G} U_0\right\}$$

for all $k \geq 1$*. As a result,*

$$\mathcal{R}_\mathcal{U} = \{P \longrightarrow \varnothing\} \cup \{G \longrightarrow G + kP : k = 1, 2, \dots\}$$

is an infinite set.

The example is further discussed in the conclusion section. Furthermore, as observed in [14], if $\mathcal{N}$ is weakly reversible and $\mathcal{U}$ is a set of non-interacting species, $\mathcal{N}_\mathcal{U}$ is not necessarily weakly reversible.

Example 3. ([14, Example 8].) *Consider the following weakly reversible reaction network with the set of non-interacting species* $\mathcal{U} = \{U_1, U_2\}$*:*

$$S_1 \longrightarrow U_1 \longrightarrow S_2 \longrightarrow U_2 \longrightarrow S_1, \quad S_3 + U_2 \rightleftharpoons S_4.$$

The reduced reaction network with $\mathcal{R}_\mathcal{U} = \{S_1 \rightleftharpoons S_2, S_2 + S_3 \longrightarrow S_4 \longrightarrow S_3 + S_1\}$ *is not weakly reversible.*

Condition 2 below is equivalent to $\mathcal{R}_\mathcal{U}$ being finite [14], and $\mathcal{N}_\mathcal{U}$ is thus a reaction network if Condition 2 is fulfilled. The proof is given in Subsection 6.1.

Condition 2. *If* $\gamma \in \Xi_i$ *for some* $i = 1, \dots, m$*, then* $\mathfrak{R}(\gamma) = (y, y)$ *for some* $y \in \mathbb{N}_0^n$*.*

Lemma 2. *The set* $\mathcal{R}_\mathcal{U}$ *is finite if and only if Condition 2 holds.*

Let $(\mathcal{N}, \lambda)$ be an SRN. We introduce a kinetics $\lambda_\mathcal{U}$ on the reduced reaction network $\mathcal{N}_\mathcal{U}$ (see [13]). For $r \in \mathcal{R}_{i,j} \subseteq \mathcal{R}$ where $i, j \in \{0, \dots, m\}$, define the function $\beta_r : \mathbb{N}_0^n \to [0, 1]$ by

$$\beta_r(x) := \lambda_r(x) \Big/ \sum_{k=0}^{m} \sum_{r' \in \mathcal{R}_{i,k}} \lambda_{r'}(x), \tag{11}$$

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with the convention $0/0 := 0$. Then

$$\sum_{k=0}^{m} \sum_{r \in \mathcal{R}_{i,k}} \beta_r(x) = \mathbf{1}_{\mathcal{D}_i}(x), \quad i = 0, \dots, m, \tag{12}$$

where

$$\mathcal{D}_i := \bigcup_{k=0}^{m} \bigcup_{r \in \mathcal{R}_{i,k}} \{x \in \mathbb{N}_0^n : x \geq \mathrm{reac}(r)\}.$$

For $\gamma \in \Xi_0$, define $\lambda^*_{\mathcal{U},\gamma} : \mathbb{N}_0^n \to \mathbb{R}_{\geq 0}$ by

$$\lambda^*_{\mathcal{U},\gamma}(x) := \lambda_{r_0}(x) \prod_{j=1}^{q} \beta_{r_j}\Big(x + \sum_{i=1}^{j} \zeta_{i-1}\Big), \tag{13}$$

where $\zeta_{i-1} := \zeta(r_{i-1})$ is the reaction vector of r_{i-1} and $i_0 = i_{q+1} := 0$. Define the kinetics $\lambda_{\mathcal{U}} = (\lambda_{\mathcal{U},r} : r \in \mathcal{R}_{\mathcal{U}})$ by

$$\lambda_{\mathcal{U},r}(x) = \sum_{\gamma \in \Xi_0 : \mathfrak{R}(\gamma) = r} \lambda^*_{\mathcal{U},\gamma}(x), \quad x \in \mathbb{N}_0^{n_{\mathcal{U}}}, \ r \in \mathcal{R}_{\mathcal{U}}. \tag{14}$$

Then $\lambda_{\mathcal{U},r}(x) > 0$ if and only if $x \geq \mathrm{reac}(r)$; see [13, Corollary 3.11]. As a consequence, $(\mathcal{N}_{\mathcal{U}}, \lambda_{\mathcal{U}})$ satisfies Condition 1. Furthermore, using Definition 7, we have

$$\sum_{r \in \mathcal{R}_{\mathcal{U}}} \lambda_{\mathcal{U},r}(x) \leq \sum_{\gamma \in \Xi_0} \lambda^*_{\mathcal{U},\gamma}(x) = \sum_{r \in \mathcal{R}} \lambda_r(x) < \infty$$

(see [13, Lemma 3.10]). This implies that the evolution of the molecule counts of the core species, $(Z(t) : t \in \mathbb{R}_{\geq 0})$, satisfies the following stochastic equation, similar to (4):

$$Z(t) = Z(0) + \sum_{r \in \mathcal{R}_{\mathcal{U}}} Y_r\Big(\int_0^t \lambda_r(Z(s))\, \mathrm{d}s\Big)\zeta(r),$$

where $(Y_r, r \in \mathcal{R}_{\mathcal{U}})$, is a (possibly infinite) collection of unit-rate independent and identically distributed Poisson processes.

Definition 8. *The pair $(\mathcal{N}_{\mathcal{U}}, \lambda_{\mathcal{U}})$ defined in Definition 7 and (14) is the reduced SRN of $(\mathcal{N}, \lambda)$ (obtained by elimination the non-interacting species in $\mathcal{U}$). In particular, if $\mathcal{R}_{\mathcal{U}}$ is finite, then $(\mathcal{N}_{\mathcal{U}}, \lambda_{\mathcal{U}})$ is an SRN.*

For example, consider the reduced reaction network in (8) and (10). We have

$$\mathfrak{R}(\gamma) = (E + A + B \longrightarrow E + P + Q),$$

where

$$\gamma = U_0 \xrightarrow{E+A \to EA} U_1 \xrightarrow{EA+B \to EAB} U_2 \xrightarrow{EAB \to E+P+Q} U_0.$$

Therefore, by (11), (13), and (14), the kinetics for the reduced reaction network is

$$\lambda_{\mathcal{U},E+A+B \to E+P+Q}(x) = \lambda^*_{\mathcal{U},\gamma}(x) = \lambda_{E+A \to EA}(x)\beta_1(x)\beta_2(x),$$

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where

$$\begin{aligned}\beta_1(x) &:= \beta_{EA+B\to EAB}(x+EA-E-A)\\ &= \frac{\lambda_{EA+B\to EAB}}{\lambda_{EA+B\to EAB}+\lambda_{EA\to E+A}}(x+EA-E-A),\\ \beta_2(x) &:= \beta_{EAB\to E+P+Q}(x-E-A-B+EAB)\\ &= \frac{\lambda_{EAB\to E+P+Q}}{\lambda_{EAB\to EA+B}+\lambda_{EAB\to E+P+Q}}(x-E-A-B+EAB).\end{aligned}$$

3. The conditional distribution as a stationary distribution

Condition 3. *If $\mathfrak{R}(\gamma)=(y+U_i, y'+U_i)$ with $\gamma\in\Xi_i$ for some $i=1,\dots,m$, then (i) $y\not\prec y'$ and (ii) $y\not\succ y'$.*

Condition 3 is a weaker version of Condition 2. If the condition is violated and $y<y'$, then the system is open with an influx of molecules or able to self-replicate [9]. Likewise, if $y'<y$, then the system is self-drainable [9]. Example 2 does not satisfy Condition 3.

Lemma 3. *Let $\mathcal{N}$ be weakly reversible, and let $\mathcal{U}$ be a set of eliminable non-interacting species. Then Condition 2 implies Condition 3.*

Below we present our main result, Theorem 1, which shows that under mild conditions, the limit stationary distribution of a complex balanced reaction network with multiscale kinetics equals the stationary distribution of its reduction by eliminating non-interacting species. Previous work [7, 13] explored related questions under stronger assumptions. The key challenge is the potentially infinite state space, preventing direct application of classic CTMC limit theorems. However, leveraging the special structure of SRNs, we prove the result using a graphical method, extending techniques from [15].

Theorem 1. *Let $(\mathcal{N},\lambda)$ be a weakly reversible SRN with a set $\mathcal{U}$ of non-interacting species satisfying Condition 3. Let $(\mathcal{N}_{\mathcal{U}},\lambda_{\mathcal{U}})$ be the reduced SRN of $(\mathcal{N},\lambda)$ by eliminating the species in $\mathcal{U}$. Let Γ be an irreducible component of $\mathcal{N}$ such that*

$$\Gamma_0 := \{x\in\Gamma : \rho(x)=0\}\neq\varnothing. \tag{15}$$

Suppose that π is a complex balanced distribution for $(\mathcal{N},\lambda)$ on Γ. Then the following hold:

(i) *Γ_0 is either an irreducible component of $\mathcal{N}_{\mathcal{U}}$ or the union of at most countably many disjoint irreducible components of $\mathcal{N}_{\mathcal{U}}$;*

(ii) *the conditional distribution π_0 of π restricted to Γ_0 is a stationary distribution for $(\mathcal{N}_{\mathcal{U}},\lambda_{\mathcal{U}})$ on Γ_0 if Γ_0 consists of a single irreducible component; otherwise, it is a linear combination of stationary distributions.*

Example 4. *Consider the reaction network $A\rightleftharpoons U$, $A+U\rightleftharpoons U$. Here, $\Gamma=\mathbb{N}_0^2\setminus\{0\}$ is the only irreducible component. Let $\mathcal{U}=\{U\}$ be a set of non-interacting species. Then*

$$\Gamma_0=\{x=(x_A,x_U)\in\Gamma : \rho(x)=x_U=0\}=\{x=(x_A,0) : x_A\in\mathbb{N}\}\simeq\mathbb{N}.$$

For a finite state space Γ, the theorem follows from [13]. The proof in the general situation is lengthy and technical, and is deferred to Subsection 6.4.

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Upon combining Lemmas 2 and 3 and Theorem 1, the next corollary follows.

Corollary 1. *If $\mathcal{N}_{\mathcal{U}}$ has finitely many reactions, then both conclusions in Theorem 1 are valid.*

3.1. A remark on Theorem 1

The proof of Theorem 1(ii) presented in Subsection 6.4 is based on the recurrence of two irreducible discrete-time Markov chains (DTMCs). Recurrence is deduced from the finiteness of the state spaces (of the DTMCs), as a result of Condition 3. The state space being finite is not a necessary condition for recurrence, and nor is recurrence necessary for the validity of Theorem 1. However, we have not been able to identify any other simple conditions that imply recurrence of these DTMCs. Condition 3 is not necessary, as demonstrated by the following (artificial) example, although Theorem 1(ii) remains valid in this particular case.

Example 5. *Consider the reaction network in Example (4),*

$$A \underset{\lambda_2}{\overset{\lambda_1}{\rightleftharpoons}} U, \quad A + U \underset{\lambda_4}{\overset{\lambda_3}{\rightleftharpoons}} U, \tag{16}$$

where for all $x = (x_A, x_U) \in \mathbb{N}_0^2$,

$$\lambda_1(x) = (x_A!)^2 \mathbf{1}_{\mathbb{N}}(x_A), \qquad \lambda_3(x) = 2[(x_A+1)!]^2 \mathbf{1}_{\mathbb{N}^2}(x_A, x_U),$$
$$\lambda_2(x) = [(x_A+1)!]^2 \mathbf{1}_{\mathbb{N}}(x_U), \qquad \lambda_4(x) = [(x_A+2)!]^2 \mathbf{1}_{\mathbb{N}}(x_U).$$

Note the unusual squared factorial rates that are instrumental for showing that Condition 3 is not necessary. The compatibility condition (Condition 1) is fulfilled, even though all rates depend on x_A. Then $\Gamma = \mathbb{N}_0^2 \setminus \{(0,0)\}$ is an irreducible component of (16). One can show that

$$\pi(x) := \frac{1}{3 \times 2^{x_A + x_U}} \quad \text{for} \quad x = (x_A, x_U) \in \Gamma$$

is a detailed balanced distribution of (16) on Γ. Therefore, Proposition 2 ensures that the reduced SRN

$$\left\{ nA \underset{\lambda_{m,n}}{\overset{\lambda_{n,m}}{\rightleftharpoons}} mA : n, m \in \mathbb{N},\ n < m \right\},$$

where $\lambda_{n,m}$ is defined in Subsection 2.3, has detailed balanced stationary distribution $\pi_0(x_A) = C\pi(x_A, 0)$, $x_A \in \mathbb{N}$, for some constant $C > 0$. In other words, Condition 3 is not necessary in Theorem 1.

Following the strategy in Step 1 of the proof of Theorem 1 (see Subsection 6.4), we construct a DTMC on $\mathcal{X} = \{x : x \geq 0\} \cup \{\partial\}$ (where ∂ is an ceremony state) with transition probabilities

$$P_{\partial,\partial} = 0, \quad P_{\partial,0} = 1, \quad P_{x,\partial} = \frac{\lambda_2(x,1)}{(\lambda_2+\lambda_3+\lambda_4)(x,1)},$$
$$P_{x,x+1} = \frac{\lambda_4(x,1)}{(\lambda_2+\lambda_3+\lambda_4)(x,1)}, \quad P_{x,x-1} = \frac{\lambda_3(x,1)}{(\lambda_2+\lambda_3+\lambda_4)(x,1)},$$

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and $P_{x,x'} = 0$ *otherwise. Then Theorem 1(ii) is valid if* $\mathbb{P}_x(\tau < \infty) = 1$, *where* $\tau := \min\{n \geq 1 : X_n = \partial\}$. *However, this is unfortunately not true. In fact, for any* $n \geq 2$,

$$\begin{aligned}\mathbb{P}_x(\tau > n) &\geq \mathbb{P}_x\big(X_k = x + k \ \forall k = 1, \ldots, n\big) \\ &= \prod_{k=1}^{n} P_{x+k-1,x+k} = \prod_{k=1}^{n} \frac{\lambda_4(x+k-1,\,1)}{(\lambda_2+\lambda_3+\lambda_4)(x+k-1,\,1)} \\ &= \prod_{k=1}^{n} \frac{\prod_{j=1}^{x+k+1} j^2}{\prod_{j=1}^{x+k} j^2 + 2\prod_{j=1}^{x+k} j^2 + \prod_{j=1}^{x+k+1} j^2} \\ &= \prod_{k=1}^{n} \left(3(x+k+1)^{-2} + 1\right)^{-1} \geq \exp\left(-3\sum_{k=1}^{\infty} x^{-2}\right) > 0,\end{aligned}$$

using that $-\log(3x^{-2} + 1) \geq -3x^{-2}$. *Therefore,* $\mathbb{P}_x(\tau = \infty) > 0$. *This implies that replicating the arguments in the proof of Theorem 1 does not suffice to show that* π_0 *is a stationary distribution for the reduced SRN. This is due to the failure of Condition 3 in (16).*

3.2. Two special cases

Assume that $\mathcal{U}$ is a set of intermediate species in a weakly reversible SRN. Then it can be demonstrated that Conditions 2 and 3 are both satisfied. Therefore Theorem 1 applies. For a set of intermediate species $\mathcal{U}$, we have that for $i, j \in \{1, \ldots, m\}$:

(i) $\mathcal{C}_i = \{U_i\}$;

(ii) $\mathcal{R}_{i,i} = \varnothing$ and $\mathcal{R}_{i,j} \subseteq \{U_i \longrightarrow U_j\}$ for $i \neq j$.

Proposition 1. *Suppose that* π *is a complex balanced distribution for* $(\mathcal{N}, \lambda)$ *on an irreducible component* Γ *and that* $\mathcal{U}$ *consists of intermediate species. Then* $\Gamma_0 := \{x \in \Gamma : \rho(x) = 0\}$ *is an irreducible component of* $(\mathcal{N}_{\mathcal{U}}, \lambda_{\mathcal{U}})$, *and* $\pi_0(\cdot) := \pi(\cdot)/\pi(\Gamma_0)$ *is a complex balanced distribution for* $(\mathcal{N}_{\mathcal{U}}, \lambda_{\mathcal{U}})$ *on* Γ_0.

Proposition 2. *Suppose that* π *is a detailed balanced distribution for* $(\mathcal{N}, \lambda)$ *on an irreducible component* Γ. *Then* $\pi_0(\cdot) := \pi(\cdot)/\pi(\Gamma_0)$ *is either a detailed balanced distribution for* $(\mathcal{N}_{\mathcal{U}}, \lambda_{\mathcal{U}})$ *on* Γ_0, *as in (15), or a linear combination of detailed balanced distributions on disjoint irreducible components.*

As noted in Subsection 2.2, a detailed balanced distribution is a complex balanced distribution, and a complex balanced distribution is a stationary distribution. Therefore, the conclusions of Propositions 1 and 2 are much stronger than those in the general case presented in Theorem 1. This is because, in the case of intermediate species or detailed balance, the reduced SRN takes a simpler form while preserving essential properties of the original SRN. The proofs of Propositions 1 and 2 are given in Subsections 6.2 and 6.3, respectively.

3.3. Positive recurrence of the reduced SRN

Theorem 2. *Let* $(\mathcal{N}, \lambda)$ *be an SRN with stochastic mass-action kinetics,* $\mathcal{U}$ *a set of non-interacting species,* $(\mathcal{N}_{\mathcal{U}}, \lambda_{\mathcal{U}})$ *the reduced SRN obtained by elimination of the species in* $\mathcal{U}$, *and* Γ *an irreducible component of* $(\mathcal{N}, \lambda)$. *Let* π *be a complex balanced stationary distribution of* $(\mathcal{N}, \lambda)$ *on* Γ, *and assume that* $\pi_0(\cdot) := \pi(\cdot)/\pi(\Gamma_0)$ *is a stationary distribution (linear combination of stationary distributions on disjoint irreducible components) of* $(\mathcal{N}_{\mathcal{U}}, \lambda_{\mathcal{U}})$ *supported*

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on $\Gamma_0 \neq \varnothing$*, as in (15). Then* $(\mathcal{N}_{\mathcal{U}}, \lambda_{\mathcal{U}})$ *is positive recurrent on each irreducible component of* Γ_0.

Proof. By assumption, π_0 is a stationary distribution on an irreducible component $\tilde{\Gamma} \subseteq \Gamma_0$. To show positive recurrence on $\tilde{\Gamma}$, we apply the sufficient condition for positive recurrence from [4, Corollary 4.4]. The condition holds if the following is true for $\tilde{\Gamma}$:

$$\sum_{z \in \tilde{\Gamma}} \sum_{r \in \mathcal{R}_{\mathcal{U}}} \lambda_{\mathcal{U},r}(z)\pi_0(z) < \infty.$$

Using that complex balanced distributions for mass-action SRNs take the form $M\frac{c^x}{x!}$ (see [2]), we can replace $\pi_0(z) = \pi(z)/\pi(\Gamma_0)$ by $M_0\frac{c^x}{x!}$ with $M_0 = M/\pi(\Gamma_0)$ and $c^x := \prod_{i=1}^n c_i^{x_i}$, for any $c \in \mathbb{R}^n_+$ and $x \in \mathbb{R}^n$. Furthermore, by Lemma 3.10 in [13],

$$\sum_{r \in \mathcal{R}_{\mathcal{U}}} \lambda_{\mathcal{U},r}(z) \leq \sum_{r \in \mathcal{R}} \lambda_r(z, 0).$$

Since $\tilde{\Gamma} \subseteq \Gamma_0 \subseteq \mathbb{N}_0^{n_{\mathcal{U}}}$ and $\mathcal{R}$ is finite, it is enough to show that

$$M_0 \sum_{z \in \mathbb{Z}^{n_{\mathcal{U}}}_{\geq 0}} \lambda_r(z, 0)\frac{c^{(z,0)}}{z!} < \infty.$$

This final inequality follows as $\lambda_r(z, 0)$ is a polynomial of fixed degree (in z) for stochastic mass-action kinetics. □

As a corollary of Theorem 1, Propositions 1 and 2, and Theorem 2, we get the following result for reductions of complex balanced SRNs with stochastic mass-action kinetics.

Corollary 2. *Let* $(\mathcal{N}, \lambda)$ *be an SRN with stochastic mass-action kinetics,* $\mathcal{U}$ *a set of non-interacting species,* $(\mathcal{N}_{\mathcal{U}}, \lambda_{\mathcal{U}})$ *the reduced SRN obtained by elimination of the species in* $\mathcal{U}$*, and* Γ *an irreducible component of* $(\mathcal{N}, \lambda)$*. Let* π *be a complex balanced stationary distribution of* $(\mathcal{N}, \lambda)$ *on* Γ*. Assume that at least one of the following conditions holds:*

- *Condition 3;*
- $\mathcal{U}$ *consists of intermediate species;*
- $\mathcal{N}$ *is reversible.*

Then $(\mathcal{N}_{\mathcal{U}}, \lambda_{\mathcal{U}})$ is positive recurrent on each irreducible component of Γ_0.

4. Convergence of complex balanced distributions

Consider an SRN $(\mathcal{N}, \lambda)$ with $\mathcal{N} = (\mathcal{S}, \mathcal{C}, \mathcal{R})$, and suppose that $\mathcal{U}$ is a proper subset of $\mathcal{S}$ with $|\mathcal{U}| = m$. In particular, $\mathcal{U}$ does not need to be a set of non-interacting species.

Let $\alpha = (\alpha_1, \ldots, \alpha_m) \in \mathbb{R}^m_{>0}$. For $N \in \mathbb{N}$, let $\lambda^\alpha_N = (\lambda^\alpha_{N,y\to y'} : y \longrightarrow y' \in \mathcal{R})$ be a kinetics on $\mathcal{N}$ defined by

$$\lambda^\alpha_{N,y\to y'} = N^{\langle \alpha, \rho(y)\rangle}\lambda_{y\to y'}, \quad y \longrightarrow y' \in \mathcal{R}, \tag{17}$$

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where ρ is the projection from $\mathbb{N}_0^n$ to $\mathbb{N}_0^m$ defined in (7). It is evident that the scaling affects only reactions that include species in $\mathcal{U}$ among their reactants.

Proposition 3. *Suppose that π is a complex balanced distribution for $(\mathcal{N}, \lambda)$ on an irreducible component Γ. Define $g_N^\alpha(x) = N^{-\langle \alpha, \rho(x)\rangle}\pi(x)$ for $N \in \mathbb{N}$. Then $M_N^\alpha = \sum_{x\in\Gamma} g_N^\alpha(x) \in (0, 1)$, and $\pi_N^\alpha(x) = \frac{1}{M_N^\alpha} g_N^\alpha(x)$ is a complex balanced distribution for $(\mathcal{N}, \lambda_N^\alpha)$ on Γ.*

Proof. Since π is a complex balanced distribution for $(\mathcal{N}, \lambda)$ on Γ, (6) states that for any $\eta \in \mathcal{C}$ and $x \in \Gamma$,

$$\pi(x) \sum_{y' :\, \eta\to y'\in\mathcal{R}} \lambda_{\eta\to y'}(x) = \sum_{y :\, y\to\eta\in\mathcal{R}} \pi(x+y-\eta)\lambda_{y\to\eta}(x+y-\eta).$$

By the definitions of λ_N^α and g_N^α and by linearity of ρ, we have

$$\begin{aligned} g_N^\alpha(x) \sum_{y' :\, \eta\to y'\in\mathcal{R}} \lambda_{N,\eta\to y'}^\alpha(x) &= N^{-\langle\alpha,\rho(x-\eta)\rangle}\pi(x) \sum_{y' \,:\, \eta\to y'\in\mathcal{R}} \lambda_{\eta\to y'}(x) \\ &= N^{-\langle\alpha,\rho(x-\eta)\rangle} \sum_{y \,:\, y\to\eta\in\mathcal{R}} \pi(x+y-\eta)\lambda_{y\to\eta}(x+y-\eta) \\ &= \sum_{y :\, y\to\eta\in\mathcal{R}} N^{-\langle\alpha,\rho(x+y-\eta)\rangle}\pi(x+y-\eta)\, N^{\langle\alpha,\rho(y)\rangle}\lambda_{y\to\eta}(x+y-\eta) \\ &= \sum_{y :\, y\to\eta\in\mathcal{R}} g_N^\alpha(x+y-\eta)\lambda_{N,y\to\eta}(x+y-\eta), \end{aligned}$$

provided that $x \geq \eta$. Furthermore, for $x \not\geq \eta$,

$$0 = g_N^\alpha(x) \sum_{y' :\, \eta\to y'\in\mathcal{R}} \lambda_{N,\eta\to y'}^\alpha(x) = \sum_{y :\, y\to\eta\in\mathcal{R}} g_N^\alpha(x+y-\eta)\lambda_{N,y\to\eta}^\alpha(x+y-\eta).$$

Note that $g_N^\alpha(x) \leq \pi(x)$ for all $x \in \Gamma$, and $g_N^\alpha(x) > 0$ if and only if $\pi(x) > 0$. This implies that $M_N^\alpha = \sum_{x\in\Gamma} g_N^\alpha(x) \in (0, 1)$ and π_N is a complex balanced distribution for $(\mathcal{N}, \lambda_N^\alpha)$ on Γ. The proof is complete. □

We have the following theorem on the asymptotic behaviour of π_N^β. It states that π_N^β converges to a probability distribution with support on a subset of Γ, which further satisfies a conservation relation.

Theorem 3. *Assume the conditions in Proposition 3. Let*

$$\gamma_0^\alpha = \min\{\langle\alpha, \rho(x)\rangle : x \in \Gamma\} \quad \text{and} \quad \Gamma_0^\alpha = \{x \in \Gamma : \langle\alpha, \rho(x)\rangle = \gamma_0^\alpha\}. \tag{18}$$

Then for every $x \in \Gamma$,

$$\pi_0^\alpha(x) = \lim_{N\to\infty} \pi_N(x) = \begin{cases} \pi(x)/\pi(\Gamma_0^\alpha) & \text{if } x \in \Gamma_0^\alpha, \\ 0 & \text{if } x \in \Gamma \setminus \Gamma_0^\alpha. \end{cases} \tag{19}$$

Intuitively, when taking $N \to \infty$, the reactions involving non-interacting species are more likely to occur prior to other reactions. Therefore, it is expected that the non-interacting species will be depleted and would reach a minimal number in the limit. This leads to the conservation

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relation γ_0^α and the state space Γ_0^α as defined in (18). Consider the reaction network (4) with $\mathcal{U} = \{U\}$. It follows that $\Gamma = \mathbb{N}_0^2 \setminus \{0\}$ is an irreducible component. For any $\alpha \in \mathbb{R}_{>0}$ we have $\gamma_0^\alpha = \min\{\langle \alpha, \rho(x)\rangle : x \in \Gamma\} = 0$, and therefore $\Gamma_0^\alpha = \{(x_A, x_U) \in \Gamma : x_U = 0\}$.

Proof. By Proposition 3, we have

$$\pi_N(x) = \frac{N^{-\langle \alpha, \rho(x)\rangle}\pi(x)}{\sum_{x' \in \Gamma} N^{-\langle \alpha, \rho(x')\rangle}\pi(x')}.$$

Decompose $\Gamma = \Gamma_0^\alpha \cup (\Gamma \setminus \Gamma_0^\alpha)$. Then it follows that

$$\sum_{x' \in \Gamma} N^{-\langle \alpha, \rho(x')\rangle}\pi(x') = \sum_{x' \in \Gamma_0^\alpha} N^{-\gamma_0^\alpha}\pi(x') + \sum_{x' \in \Gamma \setminus \Gamma_0^\alpha} N^{-\langle \alpha, \rho(x')\rangle}\pi(x'),$$

and thus

$$\begin{aligned}\pi_N(x) &= \frac{N^{-\langle \alpha, \rho(x)\rangle}\pi(x)}{\sum_{x' \in \Gamma_0^\alpha} N^{-\gamma_0^\alpha}\pi(x') + \sum_{x' \in \Gamma \setminus \Gamma_0^\alpha} N^{-\langle \alpha, \rho(x')\rangle}\pi(x')} \\ &= \frac{N^{\gamma_0^\alpha - \langle \alpha, \rho(x)\rangle}\pi(x)}{\sum_{x' \in \Gamma_0^\alpha} \pi(x') + \sum_{x' \in \Gamma \setminus \Gamma_0^\alpha} N^{\gamma_0^\alpha - \langle \alpha, \rho(x')\rangle}\pi(x')}.\end{aligned}$$

Note that Γ is an irreducible component of $\mathcal{N}$, and π is a complex balanced distribution for $(\mathcal{N}, \lambda)$. Thus, $\pi(x) > 0$ for all $x \in \Gamma$. Therefore, for $N \to \infty$, (19) follows from the fact that on the set Γ, $\gamma_0^\alpha - \langle \alpha, \rho(x')\rangle > 0$ if and only if $x' \in \Gamma \setminus \Gamma_0^\alpha$. The proof is complete. □

The distribution π_0^α in Theorem 3 is the conditional probability of π on Γ_0^α. By replacing π with π_N (defined in Proposition 3) for any N, we can conclude that π_0^α is the conditional probability of π_N^α on Γ_0. This follows from $\pi_N^\alpha(x) = N^{-\gamma_0^\alpha}\pi(x)$ for all $x \in \Gamma_0^\alpha$. In comparison with (1), Proposition 3 and Theorem 3 show that the mass-action assumption is not necessary and can be replaced by complex balancing.

As a result of Proposition 3, of Theorem 1, Proposition 1, or Proposition 2, and of Theorem 3, we have the next theorem.

Theorem 4. *Let $(\mathcal{N}, \lambda)$ be a weakly reversible SRN with a set of non-interacting species $\mathcal{U}$, and let $(\mathcal{N}, \lambda_N^\alpha)$ be the SRN with λ_N^α, for $N \in \mathbb{N}$ and $\alpha \in \mathbb{R}_{>0}^m$, as defined in (17). Suppose that π is a complex balanced distribution for $(\mathcal{N}, \lambda)$ on an irreducible component Γ and that Γ_0 defined as in (15) is non-empty. Assume that at least one of the following conditions holds:*

- *Condition 3;*
- *$\mathcal{U}$ are intermediates;*
- *$\mathcal{N}$ is reversible.*

Also, let $(\mathcal{N}_\mathcal{U}, \lambda_\mathcal{U})$ be the reduced SRN of $(\mathcal{N}, \lambda)$ by elimination of the species in $\mathcal{U}$. Then $\pi_0^\alpha = \lim_{N\to\infty} \pi_N^\alpha$, where π_0 is defined in Proposition 3, is a stationary distribution (linear combination of stationary distributions on disjoint irreducible components of $\mathcal{N}_\mathcal{U}$) of $(\mathcal{N}_\mathcal{U}, \lambda_\mathcal{U})$ supported on Γ_0.

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5. Conclusion

This paper investigates the asymptotic behaviour of complex balanced stationary distributions in a multiscale setting. It addresses a fundamental question in stochastic modelling: how the stationary distribution of a reaction network evolves when certain reaction rates are scaled by a large parameter N, leading to the rapid degradation of certain species.

A key result, presented in Theorems 1 and 3, establishes that under specific conditions, the limiting distribution of complex balanced SRNs corresponds to the stationary distribution of the reduced network obtained by eliminating non-interacting species. In particular, when the non-interacting species are intermediate species (Proposition 1), or when the original SRN is detailed balanced (Proposition 2), the limiting distributions retain their complex balanced or detailed balanced nature in the reduced reaction network. Furthermore, the results imply that under appropriate conditions, the form of the stationary distribution (Theorem 4) and positive recurrence (Corollary 2) are preserved for the reduced reaction network.

This work extends prior research [7, 13] by addressing scenarios where the reduced reaction network may lack weak reversibility or display unconventional kinetics. It would be interesting to know if there are other classes of SRNs for which a correspondence between the limiting stationary distribution and the stationary distribution of the reduced network exists. Even in simple cases it is difficult to determine the stationary distribution. Example 2 with mass-action kinetics is one such case; it is not weakly reversible, and the presence of P does not influence the stationary behaviour of G and G' (which is binomial). The stationary distribution of the full network is a Poisson mixture distribution, but the mixing measure is in general intractable [6]. If $x_G + x_{G'} = 1$, then the generating function of x_P can be expressed through Kummer's function, from which the descending factorial moments of x_P can be found [24, p. 281]. This provides a means to determine the stationary distribution of the reduced network with species G and P, but $x_G = 1$ always. By scaling the reaction rates of $G' \longrightarrow G$ and $G' \longrightarrow G' + P$ in N, the descending factorial moments of x_P in the reduced reaction network can be found. However, these do not take a familiar form [24, p. 281].

6. Proofs

In this section, we give proofs of Lemma 2, Theorem 1, and Propositions 1 and 2. In particular, the proofs of Theorem 1 and Proposition 1 extend ideas from Theorem 17 in [15]. A key step in the proofs involves verifying an identity of the form

$$x = \sum_{n=1}^{\infty} y_i \tag{20}$$

where $x > 0$ and the y_i are non-negative numbers using DTMCs. Dividing both sides of (20) by x gives an equivalent identity,

$$1 = \sum_{n=1}^{\infty} \frac{y_i}{x}. \tag{21}$$

Since $x > 0$ and the y_i are non-negative, this suggests interpreting the $\frac{y_i}{x}$ as probabilities of events that form a partition of some probability space. We associate $\frac{y_i}{x}$ with the probability of the first hitting time τ of a DTMC to a particular state, so that

$$\sum_{n=1}^{\infty} \frac{y_i}{x} = \sum_{n=1}^{\infty} \mathbb{P}(\tau = i) = \mathbb{P}(\tau < \infty).$$

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As a result, (21), and hence the original identity (20), holds if and only if the associated DTMC is recurrent.

The insight that allows us to make this association here is that β_r defined in (11) has a similar form to the transition probabilities of a DTMC, namely $\beta_r \geq 0$ and

$$\sum_{k=0}^{m} \sum_{r \in \mathcal{R}_{i,k}} \beta_r = 1.$$

We introduce some notation. Let $\mathcal{N}$ be a (reduced) reaction network. A reaction $r = y \longrightarrow y$ is an *incoming* reaction of y' and an *outgoing* reaction of y. For a complex $y \in \mathcal{C}$, $\mathrm{inc}(y)$ and $\mathrm{out}(y)$ denote the sets of all incoming and outgoing reactions of y, respectively. In a reduced reaction network, we often add the subscript $\mathcal{U}$, for example $\mathrm{out}_{\mathcal{U}}$.

For $\gamma \in \Xi_i(q)$, let

$$\mathrm{init}(\gamma) = U_i \xrightarrow{r_0} U_{i_1} \quad \text{and} \quad \mathrm{ter}(\gamma) = U_{i_q} \xrightarrow{r_q} U_i$$

be the initial and terminal edges of γ, respectively. Finally, we define

$$m_{\mathrm{pro}} := |\mathcal{U}_{\mathrm{pro}}| \quad \text{and} \quad \mathcal{U}_{\mathrm{pro}} = \{U_1, \ldots, U_{m_{\mathrm{pro}}}\} \tag{22}$$

such that $\mathcal{U} \setminus \mathcal{U}_{\mathrm{pro}} = \{U_{m_{\mathrm{pro}}+1}, \ldots, U_m\}$.

6.1. Proof of Lemma 2

($\Rightarrow$) Suppose that Condition 2 holds. Given a walk $\theta \subseteq (\mathcal{V}, \mathcal{E})$, define $\mathcal{U}_\theta := \{U_i \in \mathcal{U} : U_i \in \theta\}$. Consider a closed walk $\gamma \in \Xi_{i_0}$ for any $i_0 \in \{1, \ldots, m_{\mathrm{pro}}\}$. Then $U_{i_0} \in \mathcal{U}_\gamma$. In addition, $\mathcal{R}_{i_0,i_0} = \varnothing$, because otherwise $r = y + U_{i_0} \longrightarrow y' + U_{i_0} \in \mathcal{R}_{i_0,i_0}$ with $y \neq y'$ contradicts Condition 2. This implies $|\mathcal{U}_\gamma| \geq 2$, and

$$\mathfrak{R}(\Xi_{i_0}) = \bigcup_{k=2}^{m_{\mathrm{pro}}} A_{i_0,k}, \quad A_{i_0,k} := \{\mathfrak{R}(\gamma) : |\mathcal{U}_\gamma| = k\}.$$

We will show that $|\mathfrak{R}(\Xi_0)| < \infty$, which is the key to proving $|\mathcal{R}_{\mathcal{U}}| < \infty$.

Suppose that $k = 2$. Then γ has the form

$$\gamma = U_{i_0} \xrightarrow{r_0} U_j \xrightarrow{r_1} U_{i_0} \xrightarrow{r_2} \cdots \xrightarrow{r_{2q}} U_j \xrightarrow{r_{2q+1}} U_{i_0}$$

for some $j \in \{1, \ldots, i_0 - 1, i_0 + 1, \ldots, m_{\mathrm{pro}}\}$ and $q \in \mathbb{N}_0$. As a result of Proposition 1 from [14] and Condition 2,

$$\mathfrak{R}(\gamma) = \bigoplus_{i=0}^{q} (r_{2i} \oplus r_{2i+1}) = \bigoplus_{i=0}^{q} (y_i + U_{i_0}, y_i + U_{i_0}) \tag{23}$$

for some $y_i \in \mathbb{N}_0^{\mathcal{S}}$ with $i = 0, \ldots, q$. Note that $\{r \oplus r' : r \in \mathcal{R}_{i_0,j},\ r' \in \mathcal{R}_{j,i_0}\}$ is a finite set. This implies that

$$\left\{y \in \mathbb{N}_0^{\mathcal{S}} : (y + U_{i_0}, y + U_{i_0}) = r \oplus r',\ r \in \mathcal{R}_{i_0,j},\ r' \in \mathcal{R}_{j,i_0}\right\}$$

is a finite set. Combining this observation with Proposition 2(iii) from [14], we conclude that $A_{i_0,2}$ is finite.

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We prove finiteness of $A_{i_0,k}$ for general $k \geq 3$ by induction. Let $\gamma \in A_{i_0,k}$ be of the form (9) with $i = i_0$. It suffices to prove the claim that

$$\text{the collection of all possible } \mathfrak{R}(\gamma) \text{ is finite, assuming } i_0 \notin \{i_1, \dots, i_q\}. \tag{$*$}$$

Otherwise, we can decompose γ into a 'summation' of closed walks, where U_{i_0} only appears as the initial and terminal nodes in each closed walk. Here, we say that a walk θ is the summation of two walks θ_1 and θ_2, written as $\theta = \theta_1 + \theta_2$, if

$$\theta = U_{i_1} \xrightarrow{r_1} U_{i_2} \xrightarrow{r_2} \cdots \xrightarrow{r_{q''-1}} U_{i_{q''}},$$

$$\theta_1 = \{U_{i_1} \xrightarrow{r_1} \cdots \xrightarrow{r_{q'-1}} U_{i_{q'}}\}, \quad \text{and} \quad \theta_2 = \{U_{i_{q'}} \xrightarrow{r_{q'}} \cdots \xrightarrow{r_{q''-1}} U_{i_{q''}}\}.$$

Therefore, $\mathfrak{R}(\gamma)$ can be written in the form of (23) and finiteness of $A_{i_0,k}$ follows from [14, Proposition 2(iii)], and the finiteness of the collection of all possible y_i is finite, where the latter is a consequence of claim ($*$).

Suppose that γ of the form (9) with $i = i_0$ and $i_0 \notin \{i_1, \dots, i_q\}$. Then the collection of all possible γ can be divided into two sets,

$$B_1 := \{\gamma : i_j \neq i_{j'} \text{ for all } 1 \leq j < j' \leq q\}, \quad B_2 := \{\gamma : \gamma \text{ is not in } B_1\}.$$

It is trivial that B_1 is a finite set. It suffices to show that B_2 is finite, too. Let $\gamma \in B_2$. We decompose γ into the summation of closed walks connected by paths

$$\gamma = \theta_1 + \gamma_1 + \theta_2 + \cdots + \gamma_q + \theta_{q+1},$$

where for all i, $\gamma_i \in \Xi_{j_i'}$ and θ_i is a path in the sense that no repeated nodes are allowed.

Without loss of generality, we assume that $j_i' \neq j_{i'}'$ for all $1 \leq i < i' \leq q'$, where j_i' is such that $\gamma_i \in \Xi_{j_i'}$. Thus, $q \leq m_{\text{pro}}$. This is because, otherwise, if we let $\gamma_i' = \gamma_i + \theta_{i+1} + \cdots + \theta_{i'} + \gamma_{i'} \in \Xi_{j_i'}$ and write

$$\gamma = \theta_1 + \gamma_1 + \theta_2 + \cdots + \theta_i + \gamma_i' + \theta_{i'+1} + \gamma_{i'+1} + \cdots + \gamma_q + \theta_{q+1},$$

this process can be iterated until no repeated j_i' occurs. Note that the collection of all paths in $(\mathcal{V}, \mathcal{E})$ is finite. This implies that the collection of all possible $\mathfrak{R}(\theta_i)$ for $1 \leq i \leq q' + 1$ is finite. In addition, for any $i \in \{1, \dots, q\}$, U_{i_0} is not included in γ_i, and thus $\mathfrak{R}(\gamma_i) \in A_{j_i',k'}$ with some $k' < k$. Thanks to the induction hypothesis $|A_{j_i',k'}| < \infty$, the collection of all possible $\mathfrak{R}(\gamma_i)$ is finite for all $i = 1, \dots, q$. Hence, B_2 (the collection of all possible $\mathfrak{R}(\gamma) = \mathfrak{R}(\theta_1) \oplus \mathfrak{R}(\gamma_1) \oplus \cdots \oplus \mathfrak{R}(\theta_{q+1})$) is finite owing to [14, Proposition 2(iii)] and the fact that $q \leq m_{\text{pro}}$. This completes the proof of claim ($*$) for i_0 and thus for all $i = 1, \dots, m_{\text{pro}}$ and $k = 2, \dots, m_{\text{pro}}$.

The rest of the proof is straightforward. For any $\gamma \in \Xi_0$, we can decompose it into a summation of at most m_{pro} closed walks connected by paths. Since the ranges of the function $\mathfrak{R}$ on paths and closed walks are all finite, the collection of all possible $\mathfrak{R}(\gamma)$ is also finite. As a result, $|\mathfrak{R}(\Xi_0)| < \infty$.

($\Leftarrow$) Suppose that $\mathcal{R}_{\mathcal{U}}$ consists of finitely many reactions but Condition 2 fails. Then there exists a closed walk $\gamma_0 \in \Xi_{i_0}$ for some $i_0 \in \{1, \dots, m_{\text{pro}}\}$ such that $\mathfrak{R}(\gamma_0) = y_0 + U_{i_0} \longrightarrow y_0' + U_{i_0}$ with $y_0 \neq y_0'$. Since $\mathcal{U}_{\text{pro}} \subseteq \mathcal{U}_{\text{deg}}$ (the set $\mathcal{U}$ can be eliminated), there are paths θ_1 and θ_2 directed from U_0 to U_{i_0} and from U_{i_0} to U_0, respectively. It follows that for any $q \in \mathbb{N}$,

$$\gamma_q := \theta_1 + \gamma_q^* + \theta_2 \in \Xi_0 \quad \text{where } \gamma_q^* := \underbrace{\gamma + \cdots + \gamma}_{q \text{ instances of } \gamma}.$$

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Let $(x_q, x'_q) := \mathfrak{R}(\gamma_q)$. We will show that $\{(x_q, x'_q) : q \in \mathbb{N}\} \cap \mathcal{R}_{\mathcal{U}}$ is an infinite set. Recall that $y_0 \neq y'_0$. Without loss of generality, assume that $y_{0,1} \neq y'_{0,1}$. Here, we only prove the case of $y_{0,1} > y'_{0,1}$; the other case, $y_{0,1} < y'_{0,1}$, can be proved similarly. Let

$$(z_q + U_{i_0}, z'_q + U_{i_0}) := \mathfrak{R}(\gamma_q^*) = \bigoplus_{i=1}^{q} (y + U_{i_0}, y' + U_{i_0}).$$

Then, by Definition 3 and $y_{0,1} > y'_{0,1}$, we have

$$(z_{q,1}, z'_{q,1}) = \big(y_{0,1} + q(y_{0,1} - y'_{0,1}),\ y'_{0,1}\big).$$

This yields that $\{z_{q,1} : q \in \mathbb{N}\}$ is a strictly increasing sequence. Let $\mathfrak{R}(\theta_1) = (y_1, y'_1 + U_1)$ and $\mathfrak{R}(\theta_2) = (y_2 + U_1, y'_2)$. Then, for all $q > M$ with M large enough, $z_{q,1} \geq y'_{1,1}$ holds. As a result,

$$\begin{aligned} x_{q,1} &= y_{1,1} + z_{q,1} - y'_{0,1} + (y_{2,1} - z'_{q,1}) \vee 0 \\ &= y_{1,1} + y_{0,1} + q(y_{0,1} - y'_{0,1}) - y'_{1,1} + (y_{2,1} - y'_{0,1}) \vee 0. \end{aligned}$$

Thus, $\{x_{q,1}, q > M\}$ is a strictly increasing sequence. This contradicts $\{\mathfrak{R}(\gamma_q) = (x_q, x'_q) : q > M\} \subseteq \mathcal{R}_{\mathcal{U}}$ being a finite set. The proof is complete.

6.2. Proof of Proposition 1

If $\mathcal{U}$ consists of intermediate species, then Γ_0 is an irreducible component of $\mathcal{N}_{\mathcal{U}}$; see [14, Theorem 5.6]. In addition, if $\gamma \in \Xi_0$, then $\mathfrak{R}(\gamma) = y \longrightarrow y'$, where $y = \mathrm{reac}(r_0)$ and $y' = \mathrm{prod}(r_q)$. Thus, $\mathcal{C}_{\mathcal{U}} \subseteq \mathcal{C}_0 = \{y \in \mathcal{C} : \rho(y) = 0\}$. To prove the proposition, it suffices to show that the following equation holds for all $\eta \in \mathcal{C}_{\mathcal{U}}$ and $x \in \Gamma_0$:

$$\sum_{r \in \mathrm{out}_{\mathcal{U}}(\eta)} \pi(x)\lambda_{\mathcal{U},r}(x) = \sum_{r \in \mathrm{inc}_{\mathcal{U}}(\eta)} \pi\big(x - \zeta(r)\big)\lambda_{\mathcal{U},r}\big(x - \zeta(r)\big), \tag{24}$$

where $\mathrm{out}_{\mathcal{U}}(\eta)$ and $\mathrm{inc}_{\mathcal{U}}(\eta)$ denote the sets of outgoing and incoming reactions of η in $\mathcal{R}_{\mathcal{U}}$, respectively. If $r \in \mathfrak{R}(\Xi_0) \setminus \mathcal{R}_{\mathcal{U}}$, then $r = (\eta, \eta)$ for some η, and r is both an outgoing 'reaction' of η and an incoming 'reaction' of η, with $\zeta(r) = \eta - \eta = 0$. It follows that (24) is equivalent to

$$\sum_{r \in \mathrm{out}^*_{\mathcal{U}}(\eta)} \pi(x)\lambda_{\mathcal{U},r}(x) = \sum_{r \in \mathrm{inc}^*_{\mathcal{U}}(\eta)} \pi\big(x - \zeta(r)\big)\lambda_{\mathcal{U},r}\big(x - \zeta(r)\big), \tag{25}$$

where $\mathrm{out}^*_{\mathcal{U}}(\eta)$ and $\mathrm{inc}^*_{\mathcal{U}}(\eta)$ denote the sets of outgoing and incoming 'reactions' of η in $\mathfrak{R}(\Xi_0)$ and $\lambda_{\mathcal{U}}$ is extended to $\mathfrak{R}(\Xi_0)$ by (14).

Recall that π is a complex balanced distribution for $(\mathcal{N}, \lambda)$ and that η as in (25) is in $\mathcal{C}_{\mathcal{U}} \subseteq \mathcal{C}_0 \subseteq \mathcal{C}$. It follows that

$$\sum_{r \in \mathrm{out}(\eta)} \pi(x)\lambda_r(x) = \sum_{r \in \mathrm{inc}(\eta)} \pi\big(x - \zeta(r)\big)\lambda_r\big(x - \zeta(r)\big),$$

where $\mathrm{out}(\eta)$ and $\mathrm{inc}(\eta)$ denote the sets of outgoing and incoming reactions of η in $\mathcal{R}$.

Denote by $L_0(\eta)$ and $R_0(\eta)$ the left- and right-hand sides of (25), respectively, and by $L(\eta)$ and $R(\eta)$ the left- and right-hand sides of (24), respectively. If $x \not\geq \eta$, then $L_0(\eta) = R_0(\eta) = 0$. Thus, it suffices to show (25) assuming $x \geq \eta$.

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Step 1: $L(\eta) = L_0(\eta)$. We have

$$L(\eta) = \pi(x)\left(\sum_{r\in\mathrm{out}(\eta)\cap\mathcal{R}_{0,0}} \lambda_r(x) + \sum_{i=1}^{m_{\mathrm{pro}}} \sum_{r\in\mathrm{out}(\eta)\cap\mathcal{R}_{0,i}} \lambda_r(x)\right)$$

and

$$\begin{aligned} L_0(\eta) =& \pi(x) \sum_{\gamma\in\Xi_0:\, g(\gamma)=\eta} \lambda^*_\gamma(x) \\ =& \pi(x)\left(\sum_{r\in\mathrm{out}(\eta)\cap\mathcal{R}_{0,0}} \lambda_r(x) + \sum_{k=1}^{\infty} \sum_{\gamma\in\Xi_0(k):\, g(\gamma)=\eta} \lambda^*_\gamma(x)\right), \end{aligned}$$

where m_{pro} is given in (22) and $g(\gamma) := \mathrm{reac}(\mathrm{init}(\gamma))$ is the reactant of the reaction of the initial edge of γ. We claim that for any reaction $r_* = \eta \xrightarrow{r_*} U_\iota$ with $U_\iota \in \mathcal{U}_{\mathrm{pro}}$,

$$\lambda_{r_*}(x) = \sum_{k=1}^{\infty} \sum_{\gamma\in\Xi_0(k):\, \mathrm{init}(\gamma)=U_0\xrightarrow{r_*}U_\iota} \lambda^*_\gamma(x). \tag{26}$$

Then, by summing both sides of (26) over $r_* \in \mathrm{out}(\eta)\setminus\mathcal{R}_{0,0}$, we get

$$\sum_{r_*\in\mathrm{out}(\eta)\setminus\mathcal{R}_{0,0}} \lambda_{r_*}(x) = \sum_{\gamma\in\Xi_0:\, g(\gamma)=\eta} \lambda^*_\gamma(x)$$

and thus $L(\eta) = L_0(\eta)$.

To prove (26), we construct an auxiliary DTMC X on $\mathcal{X} = \{U_0\}\cup\mathcal{U}_{\mathrm{pro}}$. By (12), the transition probabilities can be defined as

$$\mathbb{P}_{U_i}(U_j) = P_{i,j} = \sum_{r\in\mathcal{R}_{i,j}} \beta_r\big(x-\eta+\mathrm{reac}(r)\big).$$

Thus, for any $i, j \in \{0,\dots,m_{\mathrm{pro}}\}$, $P_{i,j} > 0$ if and only if $U_i \longrightarrow U_j \in \mathcal{R}$. In addition, since $\mathcal{U}$ is eliminable, it follows that X is irreducible. Let $\tau = \min\{k \ge 1 : X_k = U_0\}$. Note that

$$\begin{aligned} \mathbb{P}_{U_\iota}(\tau=1) = P_{\iota,0} =& \sum_{r\in\mathcal{R}_{\iota,0}} \beta_r(x-\eta+U_\iota) = \lambda_{r_*}(x)^{-1} \sum_{r\in\mathcal{R}_{\iota,0}} \lambda_{r_*}(x)\beta_r(x-\eta+U_\iota) \\ =& \lambda_{r_*}(x)^{-1} \sum_{\gamma\in\Xi_0(1):\, \mathrm{init}(\gamma)=U_0\xrightarrow{r_*}U_\iota} \lambda^*_\gamma(x). \end{aligned}$$

By iteration, one can show that for every $k \in \mathbb{N}$,

$$\mathbb{P}_{U_\iota}(\tau=k) = \lambda_{r_*}(x)^{-1} \sum_{\gamma\in\Xi_0(k):\, \mathrm{init}(\gamma)=U_0\xrightarrow{r_*}U_\iota} \lambda^*_\gamma(x).$$

Taking (13) into account and using that the Markov chain is irreducible (cf. [23, Theorems 1.5.6 and 1.5.7]), we have

$$1 = \mathbb{P}_{U_\iota}(\tau<\infty) = \sum_{k=1}^{\infty} \mathbb{P}_{U_\iota}(\tau=k) = \lambda_{r_*}(x)^{-1} \sum_{k=1}^{\infty} \sum_{\gamma\in\Xi_0(k):\, \mathrm{init}(\gamma)=U_0\xrightarrow{r_*}U_\iota} \lambda^*_\gamma(x).$$

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This proves (26) and thus $L(\eta) = L_0(\eta)$.

Step 2: $R(\eta) = R_0(\eta)$. Similarly, in order to show that $R(\eta) = R_0(\eta)$, it suffices to verify that for any $r^* = U_\iota \xrightarrow{r^*} \eta$ with some $U_\iota \in \mathcal{U}_{\mathrm{deg}} = \mathcal{U}_{\mathrm{pro}}$ (see Lemma 1), the following equation holds:

$$\begin{aligned}&\pi(x-\eta+U_\iota)\lambda_{r^*}(x-\eta+U_\iota)\\&\quad=\sum_{k=1}^{\infty}\sum_{\gamma\in\Xi_0(k):\,\mathrm{ter}(\gamma)=U_\iota\xrightarrow{r^*}U_0}\pi\big(x-\zeta(\mathfrak{R}(\gamma))\big)\lambda_\gamma^*\big(x-\zeta(\mathfrak{R}(\gamma))\big).\end{aligned}\tag{27}$$

For any $i, j \in \{0, \dots, m_{\mathrm{pro}}\}$, let

$$P_{i,j} = \begin{cases} \dfrac{\sum_{y:\, y\to\eta\in\mathcal{R}_{j,0}} \pi(x-\eta+y)\lambda_{y\to\eta}(x-\eta+y)}{\pi(x)\sum_{y':\,\eta\to y'\in\mathcal{R}}\lambda_{\eta\to y'}(x)}, & i=0,\\ \dfrac{\sum_{r\in\mathcal{R}_{j,i}}\pi(x-\eta+\mathrm{reac}(r))\lambda_r(x-\eta+\mathrm{reac}(r))}{\pi(x-\eta+U_i)\sum_{y':\,U_i\to y'\in\mathcal{R}}\lambda_{U_i\to y'}(x-\eta+U_i)}, & i\neq 0.\end{cases}$$

Recall that π is a complex balanced distribution for $(\mathcal{N}, \lambda)$ on $\mathcal{N}$; then, from (6) and Condition 1, we see that $\mathbb{P}_{U_i}(U_j) = P_{i,j}$ for $i, j \in \{0, \dots, m_{\mathrm{pro}}\}$ forms a transition probability for a DTMC, say Y, on $\mathcal{X}$. Let $\tau := \min\{q \geq 1 \colon Y_q = U_0\}$, and for any $k \in \mathbb{N}$ let

$$R_{1,k}(\eta) := \sum_{\gamma\in\Xi_0(k):\,\mathrm{ter}(\gamma)=U_\iota\xrightarrow{r^*}U_0}\pi\big(x-\zeta(\mathfrak{R}(\gamma))\big)\lambda_\gamma^*\big(x-\zeta(\mathfrak{R}(\gamma))\big).$$

We aim to show that

$$\mathbb{P}_{U_\iota}(\tau = k) = R_{1,k}(\eta)/L_1(\eta)\tag{28}$$

for all $k \geq 1$, where $L_1(\eta)$ is the left-hand side of (27). Suppose that $k = 1$. Then

$$\mathbb{P}_{U_\iota}(\tau=1) = P_{\iota,0} = \frac{\sum_{r\in\mathcal{R}_{0,\iota}}\pi(x-\eta+\mathrm{reac}(r))\lambda_r(x-\eta+\mathrm{reac}(r))}{\pi(x-\eta+U_\iota)\sum_{y':\,U_i\to y'\in\mathcal{R}}\lambda_{U_i\to y'}(x-\eta+U_i)}.\tag{29}$$

On the other hand, for any $r' = y \longrightarrow y' \in \mathcal{R}_{i,j}$ with some $i, j \in \{0, \dots, m_{\mathrm{pro}}\}$ and $x' \geq y$, it follows from (11) and (12) that

$$\lambda_{r'}(x') = \lambda_{r'}(x')\sum_{j'=0}^{m}\sum_{r''\in\mathcal{R}_{i,j'}}\beta_{r''}(x') = \beta_{r'}(x')\sum_{j'=0}^{m}\sum_{r''\in\mathcal{R}_{i,j'}}\lambda_{r''}(x') > 0$$

and therefore

$$\beta_{r'}(x') = \lambda_{r'}(x')\Big/\sum_{j'=0}^{m}\sum_{r''\in\mathcal{R}_{i,j'}}\lambda_{r''}(x').\tag{30}$$

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As a consequence, we have

$$R_{1,1}(\eta) = \sum_{y:\, y\to U_\iota\in\mathcal{R}_{0,\iota}} \pi(x-\eta+y)\lambda_{y\to U_\iota}(x-\eta+y)\beta_{r^*}(x-\eta+y-y+U_\iota)$$
$$= \frac{\lambda_{r^*}(x-\eta+U_\iota)\sum_{y:\, y\to U_\iota\in\mathcal{R}_{0,\iota}} \pi(x-\eta+y)\lambda_{y\to U_\iota}(x-\eta+y)}{\sum_{y':\, U_\iota\to y'\in\mathcal{R}} \lambda_{U_\iota\to y'}(x-\eta+U_\iota)}. \tag{31}$$

By comparing (27), (29), and (31), one obtains equation (28) with $k=1$.

Similarly, assume $k=2$. Then we can write

$$\mathbb{P}_{U_\iota}(\tau=2) = \sum_{i=1}^{m_{\mathrm{pro}}} \sum_{y:\, y\to U_i\in\mathcal{R}_{0,i}} \Bigg[\frac{\pi(x+\eta-y)\lambda_{y\to U_i}(x-\eta+y)}{\sum_{y':\, U_i\to y'\in\mathcal{R}} \lambda_{U_i\to y'}(x)}$$
$$\times \frac{\lambda_{U_i\to U_\iota}(x-\eta+U_i)}{\pi(x-\eta+U_\iota)\sum_{y':\, U_\iota\to y'\in\mathcal{R}} \lambda_{U_\iota\to y'}(x-\eta+U_\iota)}\Bigg],$$

and using (30) we have

$$R_{1,2}(\eta) = \sum_{i=1}^{m_{\mathrm{pro}}} \sum_{y:\, y\to U_i\in\mathcal{R}_{0,i}} \Big[\pi(x-\eta+y)\lambda_{y\to U_i}(x-\eta+y)$$
$$\times\ \beta_{U_i\to U_\iota}(x-\eta+U_i)\beta_{r^*}(x-\eta+U_\iota)\Big]$$
$$= \Bigg[\sum_{i=1}^{m_{\mathrm{pro}}} \sum_{y:\, y\to U_i\in\mathcal{R}_{0,i}} \frac{\lambda_{y\to U_i}(x-\eta+y)\lambda_{U_i\to U_\iota}(x-\eta+U_i)}{\sum_{y':\, U_i\to y'\in\mathcal{R}} \lambda_{U_i\to y'}(x-\eta+U_i)}\Bigg]$$
$$\times \frac{\lambda_{U_\iota\to\eta}(x-\eta+U_\iota)}{\sum_{y':\, U_\iota\to y'\in\mathcal{R}} \lambda_{U_\iota\to y'}(x-\eta+U_\iota)}.$$

This implies that equation (28) holds with $k=2$ as well. By using an iteration argument, one should be convinced that (28) is true for all $k\in\mathbb{N}$. This leads to (27) and hence $R_0(\eta)=R(\eta)$. The proof of this proposition is complete.

6.3. Proof of Proposition 2

The reduced reaction network $\mathcal{N}_{\mathcal{U}}$ is reversible; see [14, Theorem 5.1]. For $\gamma\in\Xi_0$, by reversibility, there exists the walk in the opposite direction,

$$\gamma' = U_0 \xrightarrow{r'_q} U_{i_q} \longrightarrow \cdots \xrightarrow{r'_1} U_1 \xrightarrow{r'_0} U_0 \ \in \Xi_0,$$

where $r'_j = y' \longrightarrow y$ if $r_j = y \longrightarrow y'$ for $0\le j\le q$ with $i_0 = i_{q+1} = 0$. This implies that $\zeta(r_j) = -\zeta(r'_j)$ for all $0\le j\le q$, and thus $\zeta(\gamma) = -\zeta(\gamma')$ with $\zeta(\gamma) := \sum_{j=0}^{q}\zeta(r_j)$. For any $x\in\Gamma_0$, define

$$x' := x+\zeta(\gamma) = x+\sum_{j=0}^{q}\zeta(r_j) = x-\sum_{j=0}^{q}\zeta(r'_j) = x-\zeta(\gamma').$$

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By (14), it is enough to verify the following equation:

$$\pi(x)\lambda^*_\gamma(x) = \pi(x')\lambda^*_{\gamma'}(x'), \tag{32}$$

provided that $x \geq \mathrm{reac}(\Re(\gamma))$. Recall that π is a detailed balanced distribution for $(\mathcal{N}, \lambda)$. By definition,

$$\pi(x)\lambda_{r_j}(x) = \pi\big(x - \zeta(r'_j)\big)\lambda_{r'_j}\big(x - \zeta(r'_j)\big) = \pi\big(x + \zeta(r_j)\big)\lambda_{r'_j}\big(x + \zeta(r_j)\big).$$

Therefore,

$$\begin{aligned}
\pi(x)\lambda^*_\gamma(x) &= \pi(x)\lambda_{r_0}(x)\prod_{j=1}^{q}\frac{\lambda_{r_j}\big(x+\zeta(r_0)+\cdots+\zeta(r_{j-1})\big)}{\sum_{j'=0}^{m}\sum_{r\in\mathcal{R}_{i_j,j'}}\lambda_r\big(x+\zeta(r_0)+\cdots+\zeta(r_{j-1})\big)}\\
&= \lambda_{r'_0}\big(x+\zeta(r_0)\big)\pi\big(x+\zeta(r_0)\big)\frac{\lambda_{r_1}\big(x+\zeta(r_0)\big)}{\sum_{j'=0}^{m}\sum_{r'\in\mathcal{R}_{i_1,j'}}\lambda_{r'}\big(x+\zeta(r_0)\big)}\\
&\quad\times\prod_{j=2}^{q}\frac{\lambda_{r_j}\big(x+\zeta(r_0)+\cdots+\zeta(r_{j-1})\big)}{\sum_{j'=0}^{m}\sum_{r''\in\mathcal{R}_{i_j,j'}}\lambda_{r''}\big(x+\zeta(r_0)+\cdots+\zeta(r_{j-1})\big)}\\
&= \beta_{r'_0}\big(x'+\zeta(r'_q)+\cdots+\zeta(r'_1)\big)\pi\big(x+\zeta(r_0)\big)\lambda_{r_1}\big(x+\zeta(r_0)\big)\\
&\quad\times\prod_{j=2}^{q}\frac{\lambda_{r_j}\big(x+\zeta(r_0)+\cdots+\zeta(r_{j-1})\big)}{\sum_{j'=0}^{m}\sum_{r''\in\mathcal{R}_{i_j,j'}}\lambda_{r''}\big(x+\zeta(r_0)+\cdots+\zeta(r_{j-1})\big)}.
\end{aligned}$$

Similarly, we deduce that

$$\begin{aligned}
&\pi\big(x+\zeta(r_0)\big)\lambda_{r_1}\big(x+\zeta(r_0)\big)\prod_{j=2}^{q}\frac{\lambda_{r_j}\big(x+\zeta(r_0)+\cdots+\zeta(r_{j-1})\big)}{\sum_{j'=0}^{m}\sum_{r\in\mathcal{R}_{i_j,j'}}\lambda_r\big(x+\zeta(r_0)+\cdots+\zeta(r_{j-1})\big)}\\
&= \beta_{r'_1}\big(x'+\zeta(r'_q)+\cdots+\zeta(r'_2)\big)\pi\big(x+\zeta(r_0)+\zeta(r_1)\big)\lambda_{r_2}\big(x+\zeta(r_0)+\zeta(r_1)\big)\\
&\quad\times\prod_{j=3}^{q}\frac{\lambda_{r_j}\big(x+\zeta(r_0)+\cdots+\zeta(r_{j-1})\big)}{\sum_{j'=0}^{m}\sum_{r'\in\mathcal{R}_{i_j,j'}}\lambda_{r'}\big(x+\zeta(r_0)+\cdots+\zeta(r_{j-1})\big)}.
\end{aligned}$$

Upon repeating the above arguments, one ends up with the equation

$$\pi(x)\lambda^*_\gamma(x) = \pi(x')\lambda^*_{\gamma'}(x')\prod_{j=1}^{q}\beta_{r'_{j-1}}\left(x'+\sum_{j'=j}^{q}\zeta(r'_{j'})\right) = \pi(x')\lambda^*_{\gamma'}(x').$$

This proves (32), and thus π_0 is a detailed balanced distribution (or linear combination of detailed balanced distributions) for $(\mathcal{N}_\mathcal{U}, \lambda_\mathcal{U})$ on Γ_0. The proof is complete.

6.4. Proof of Theorem 1

Proof of (i). It suffices to show that for any $x \in \Gamma_0$ and $x' \in \mathbb{N}_0^{n_\mathcal{U}}$, $x \to_{\mathcal{N}_\mathcal{U}} x'$ implies (a) $x' \in \Gamma_0$ and (b) $x' \to_{\mathcal{N}_\mathcal{U}} x$.

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By definition, $x \to_{\mathcal{N}_\mathcal{U}} x'$ if and only if there exist reactions $r_1, \dots, r_k \in \mathcal{R}_\mathcal{U}$ such that $r_1 \oplus \cdots \oplus r_k = (y, y')$ with $x \geq y$ and $x' - x = y' - y$. Using an iteration argument, we can assume that $k = 1$. By the definition of the reduction of reaction networks, either $r_1 \in \mathcal{R}$ or there exists a $\gamma \in \Xi_0$ such that $r_1 = \mathfrak{R}(\gamma)$. In either case, we have $x \to_\mathcal{N} x'$ with $\rho(x') = 0$ and thus $x' \in \Gamma_0$.

By the weak reversibility of $\mathcal{N}$, if $r_1 = y_1 \longrightarrow y' \in \mathcal{R}$, then there exists a sequence of reactions such that $y' \longrightarrow y_1 \longrightarrow y_2 \longrightarrow \cdots \longrightarrow y_{k'} \longrightarrow y \subseteq \mathcal{R}$. We further assume that $y_i \neq y_j$ for all $1 \leq i < j \leq k'$. Otherwise, if $y_i = y_j$, one can work with the sequence $y' \longrightarrow y_1 \longrightarrow \cdots \longrightarrow y_i \longrightarrow y_{j+1} \longrightarrow \cdots \longrightarrow y$, which is also included in $\mathcal{R}$. If $y_i \in \mathcal{C}_0$ for all $i = 1, \dots, k'$, then each reaction is also an element of $\mathcal{R}_\mathcal{U}$. This proves $x' \to_{\mathcal{N}_\mathcal{U}} x$. Otherwise, there are $1 \leq i_1 < i_2 < \cdots < i_{k''} \leq k'$ for some $k'' < k'$ such that $y_i \in \mathcal{C}_0$ if and only if $i \in \{i_1, \dots, i_{k''}\}$. For each $q \in \{0, \dots, k''\}$, let γ_q be the closed walk in $(\mathcal{V}, \mathcal{E})$ given by the reactions $y_{i_q} \longrightarrow y_{i_q+1} \longrightarrow \cdots \longrightarrow y_{i_{q+1}}$, where by convention $y_{i_0} := y'$ and $y_{i_{k'+1}} := y$. Then $\gamma_q \in \Xi_0$ for all q. By removing all γ_q such that $\mathfrak{R}(\gamma_q) = (y, y)$ for some $y \in \mathbb{N}_0^n$ and recalling the assumption that $y_i \neq y_j$ for all $1 \leq i < j \leq k'$, we know that $r_{(q)} := \mathfrak{R}(\gamma_q) = y_{i_q} \longrightarrow y_{i_{q+1}} \in \mathcal{R}_\mathcal{U}$. Therefore $\bigoplus_{q=0}^{k''} r_{(q)} = (y', y)$. This proves $x' \to_{\mathcal{N}_\mathcal{U}} x$. The proof of Theorem 1(i) is thus complete. □

Proof of (ii). For any $\eta \in \mathcal{C}_0$, let

$$\begin{aligned} L_0(\eta) &= \sum_{r \in \mathrm{out}^*_\mathcal{U}(\eta)} \pi(x) \lambda_{\mathcal{U},r}(x) \\ &= \sum_{r \in \mathrm{out}(\eta) \cap \mathcal{R}_{0,0}} \pi(x) \lambda_r(x) + \sum_{\gamma \in \Xi_0 \colon \mathrm{init}(\gamma) \in \mathrm{out}(\eta)} \pi(x) \lambda^*_\gamma(x), \end{aligned}$$

$$\begin{aligned} R_0(\eta) = &\sum_{r \in \mathrm{inc}(\eta) \cap \mathcal{R}_{0,0}} \pi\big(x - \zeta(r)\big) \lambda_r\big(x - \zeta(r)\big) \\ &+ \sum_{\gamma \in \Xi_0 \colon \mathrm{ter}(\gamma) \in \mathrm{inc}(\eta)} \pi\big(x - \zeta(\mathfrak{R}(\gamma))\big) \lambda^*_\gamma\big(x - \zeta(\mathfrak{R}(\gamma))\big), \end{aligned}$$

where $x \in \Gamma_0$ satisfies $x \geq \eta$. We use $L(\eta)$ and $R(\eta)$ to denote the left- and right-hand sides, respectively, of the following complex balanced equation:

$$\pi(x) \sum_{r \in \mathrm{out}(\eta)} \lambda_r(x) = \sum_{r \in \mathrm{inc}(\eta)} \pi\big((x - \zeta(r)\big) \lambda_r\big(x - \zeta(r)\big).$$

Then we prove $L_0(\eta) = R_0(\eta)$ by verifying that $L(\eta) = L_0(\eta)$ and $R(\eta) = R_0(\eta)$. Once this has been done, because $L_0(\eta) = R_0(\eta) = 0$ if $x \not\geq \eta$, we have

$$\pi(x) \sum_{r \in \mathfrak{R}(\Xi_0)} \lambda_{\mathcal{U},r}(x) = \sum_{\eta \in \mathcal{C}_0} L_0(\eta) = \sum_{\eta \in \mathcal{C}_0} R_0(\eta) = \sum_{r \in \mathfrak{R}(\Xi_0)} \pi\big(x - \zeta(r)\big) \lambda_{\mathcal{U},r}\big(x - \zeta(r)\big).$$

This implies that

$$\pi(x) \sum_{r \in \mathcal{R}_\mathcal{U}} \lambda_{\mathcal{U},r}(x) = \sum_{r \in \mathcal{R}_\mathcal{U}} \pi\big(x - \zeta(r)\big) \lambda_{\mathcal{U},r}\big(x - \zeta(r)\big),$$

and thus π is a stationary distribution for $(\mathcal{N}_\mathcal{U}, \lambda_\mathcal{U})$.

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To achieve this goal, we introduce two DTMCs, which are used in the proofs of $L(\eta) = L_0(\eta)$ and $R(\eta) = R_0(\eta)$. Denote by Θ_0 the set of all open (not closed) walks in $(\mathcal{V}, \mathcal{E})$ of the form

$$\theta = \left\{ U_0 \xrightarrow{r_0} U_{i_1} \xrightarrow{r_1} \cdots \xrightarrow{r_{q-1}} U_{i_q} \right\}, \quad q \in \mathbb{N}_0,\ i_1, \dots, i_q \in \{1, \dots, m_{\text{pro}}\}.$$

Define $\mathcal{X} := \mathcal{X}_0 \cup \{\partial\}$, where ∂ is a ceremony state, and

$$\mathcal{X}_0 := \left\{ x + \zeta(\mathfrak{R}(\theta)) \colon \theta \in \Theta_0,\ x \geq \operatorname{reac}(\mathfrak{R}(\theta)) \right\}. \tag{33}$$

Analogously, define $\mathcal{Y} := \mathcal{Y}_0 \cup \{\partial\}$, where

$$\mathcal{Y}_0 := \left\{ y \in \mathbb{N}_0^n \colon y + \zeta(\mathfrak{R}(\theta)) = x,\ \theta \in \Theta_0',\ y \geq \operatorname{reac}(\mathfrak{R}(\theta)) \right\}, \tag{34}$$

with Θ_0' consisting of all open walks in $(\mathcal{V}, \mathcal{E})$ of the form

$$\theta = \{ U_{i_1} \xrightarrow{r_1} \cdots \xrightarrow{r_{q-1}} U_{i_q} \xrightarrow{r_q} U_0 \}, \quad q \in \mathbb{N}_0,\ i_1, \dots, i_q \in \{1, \dots, m_{\text{pro}}\}.$$

Lemma 4.

(i) *$\mathcal{X}_0$ in (33) is finite for any $x \in \mathbb{N}_0^n$ if and only if Condition 3(i) holds.*

(ii) *$\mathcal{Y}_0$ in (34) is finite for any $x \in \mathbb{N}_0^n$ if and only if Condition 3(ii) holds.*

The proof of Lemma 4 is in Subsection 6.5.

Step 1: $L(\eta) = L_0(\eta)$. As in Step 1 of Subsection 6.2, to prove $L(\eta) = L_0(\eta)$ it suffices to show that for every reaction $r_* = \eta \longrightarrow y' + U_\iota \in \mathcal{R}_{0,\iota}$,

$$\sum_{k=1}^{\infty} \sum_{\gamma \in \Xi_0(k) \colon \operatorname{init}(\gamma) = r_*} \lambda_\gamma^*(x) = \lambda_{r_*}(x). \tag{35}$$

To prove (35), we introduce a DTMC X and relate (35) to the recurrence of X. For a clearer understanding, we refer readers to Subsection 6.2, where a simpler instance is detailed to illustrate how the recurrence of X leads to the validity of (35). Because of the non-interacting structure, for any $z \in \mathcal{X}_0$ we have $\rho(z) = U_i$ for some $U_i \in \mathcal{U}_{\text{pro}}$. This allows us to define the transition probabilities of the Markov chain X as follows:

$$\mathbb{P}_z(z') = P_{z,z'} := \begin{cases} \displaystyle\sum_{r \in \mathcal{R}_{0,0}} \beta_r(x), & z = z' = \partial, \\ \displaystyle\sum_{r \in \mathcal{R}_{i,0}} \beta_r(z), & \rho(z) = U_i,\ z' = \partial, \\ \displaystyle\sum_{r \in \mathcal{R}_{0,j} \colon \zeta(r) = z' - x} \beta_r(x), & z = \partial,\ \rho(z') = U_j, \\ \displaystyle\sum_{r \in \mathcal{R}_{i,j} \colon \zeta(r) = z' - z} \beta_r(z), & \rho(z) = U_i,\ \rho(z') = U_j, \end{cases}$$

where $i, j \in \{1, \dots, m_{\text{pro}}\}$. Moreover, (35)

$$\mathbb{P}_{x + \zeta(r_0)}(\tau < \infty) = 1, \quad \text{where } \tau = \min\{k \geq 1 : X_k = \partial\}. \tag{36}$$

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By weak reversibility of $\mathcal{N}$, X is irreducible, and thus (36) is true because $\mathcal{X}_0$ is a finite set; see Lemma 4(i).

Step 2: $R(\eta) = R_0(\eta)$. Using the same idea as in Step 2 of Subsection 6.2, we can reduce this task to showing that for every reaction $r^* = y' + U_\iota \longrightarrow \eta \in \mathcal{R}_{\iota,0}$,

$$\sum_{\gamma\in\Xi_0,\ \mathfrak{R}(\mathrm{ter}(\gamma))=r^*} \pi\big(x-\zeta(\mathfrak{R}(\gamma))\big)\lambda^*_\gamma\big(x-\zeta(\mathfrak{R}(\gamma))\big) = \pi\big(x-\zeta(r^*)\big)\lambda_{r^*}\big(x-\zeta(r^*)\big) \tag{37}$$

for all $x \in \Gamma_0$ such that $x - \zeta(r^*) \geq \mathrm{reac}(r^*)$.

Let Y be a DTMC on $\mathcal{Y}$ with transition probabilities

$$P_{z,z'} = \begin{cases} \displaystyle\sum_{r\in\mathcal{R}_{0,0}} \frac{\pi\big(x-\zeta(r)\big)\lambda_{y\to z}\big(x-\zeta(r)\big)}{\pi(x)\sum_{j=0}^m \sum_{r'\in\mathcal{R}_{0,j}} \lambda_{r'}(x)}, & z = z' = \partial, \\ \displaystyle\sum_{r\in\mathcal{R}_{i,0}:\ \zeta(r)=z'-x} \frac{\pi(z')\lambda_r(z')}{\pi(x)\sum_{j=0}^m \sum_{r'\in\mathcal{R}_{0,j}} \lambda_{r'}(x)}, & z = \partial,\ \rho(z') = U_i, \\ \displaystyle\sum_{r\in\mathcal{R}_{0,j}} \frac{\pi\big(z-\zeta(r)\big)\lambda_r\big(z-\zeta(r)\big)}{\pi(z)\sum_{j'=0}^m \sum_{r'\in\mathcal{R}_{j,j'}} \lambda_{r'}(z)}, & \rho(z) = U_j,\ z' = \partial, \\ \displaystyle\sum_{r\in\mathcal{R}_{i,j}:\ \zeta(r)=z'-z} \frac{\pi(z')\lambda_r(z')}{\pi(z)\sum_{j'=0}^m \sum_{r'\in\mathcal{R}_{j,j'}} \lambda_{r'}(z)}, & \rho(z) = U_j,\ z' = U_i, \end{cases}$$

where $i, j \in \{1, \ldots, m_{\mathrm{pro}}\}$. Following the same line of argument as in Step 2 of Subsection 6.2, we can show that (37) is equivalent to $\mathbb{P}_{y'+U_i}(\tau < \infty) = 1$, where $\tau := \min\{k \geq 1 \colon Y_k = \partial\}$. This is due to the recurrence of an irreducible DTMC in a finite state space. The proof of Theorem 1(ii) is thus complete. □

6.5. Proof of Lemma 4

It suffices to show Lemma 4(i) by proving the following statements.

(A) If Condition 3(i) fails, then $\mathcal{X}_0$ in (33) is infinite for some $x \in \mathbb{N}_0^n$.

(B) If Condition 3(i) holds, then $\mathcal{X}_0$ in (33) is finite for all $x \in \mathbb{N}_0^n$.

Proof of statement (A). Suppose that Condition 3(i) fails; then there exists $\gamma \in \Xi_i$ such that $\mathfrak{R}(\gamma) = (y + U_i, y' + U_i) \in \Xi_i$ for some $U_i \in \mathcal{U}_{\mathrm{pro}}$ and $y < y'$. Since $U_i \in \mathcal{U}_{\mathrm{pro}}$, there exists a walk θ in $(\mathcal{V}, \mathcal{E})$ with $\mathrm{init}(\theta) = U_0$ and $\mathrm{ter}(\theta) = U_i$. Consider the sequence of paths

$$\theta_q := \theta + \underbrace{\gamma + \cdots + \gamma}_{q \text{ instances of } \gamma} \in \Theta_0, \quad q \geq 1.$$

Let $\mathfrak{R}(\theta) = (y_0, y_0')$. Then

$$(z_q, z_q') := \mathfrak{R}(\theta_q) = \mathfrak{R}(\theta) \oplus \underbrace{\mathfrak{R}(\gamma) \oplus \cdots \oplus \mathfrak{R}(\gamma)}_{q \text{ instances of } \mathfrak{R}(\gamma)} = (y_0, y_0') \oplus (y, y + q(y' - y)).$$

Using Proposition 2(4) from [14], we have $z_q \leq y_0 + y_1$ and $z_q' \geq y + q(y' - y)$. It follows that the set

$$\big\{x + \zeta\big(\mathfrak{R}(\theta_q)\big) = y_0 + z_q' - z_q \colon q \in \mathbb{N}\big\}$$

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is an infinite subset of $\mathcal{X}_0$. This completes the proof of statement (A). □

The proof of statement (B) is based on the next two lemmas.

Lemma 5. *Let n be a positive integer and let $\{x_n\}_{n\geq 1} \subseteq \mathbb{R}^n$ be a sequence of vectors that is bounded from below. Then there exists a non-decreasing subsequence $\{x_{n_k}\}_{k\geq 1}$ of $\{x_n\}_{n\geq 1}$. Moreover, if $x_n \neq x_m$ for all $n \neq m$, $\{x_{n_k}\}_{k\geq 1}$ is strictly increasing.*

Lemma 6. *Let $x \in \mathbb{N}_0^n$, let q be a positive integer, and let $\mathcal{Z} := \{\zeta_1, \ldots, \zeta_q\} \subseteq \mathbb{Z}^n \setminus \mathbb{N}_0^n$. Let $\mathcal{H}$ consist of all linear combinations of elements in $\mathcal{Z}$ with non-negative integer coefficients,*

$$\mathcal{H} := \left\{ \sum_{i=1}^{q} k_i \zeta_i \colon k = (k_1, \ldots, k_q) \in \mathbb{N}_0^q \right\}.$$

Then (i) $\mathcal{H}_x := \{\eta \in \mathcal{H} : x + \eta \in \mathbb{N}_0^n\}$ is a finite set if and only if (ii) $\mathcal{H} \cap \mathbb{N}_0^n \setminus \{0\} = \varnothing$.

Remark 1. Although we believe that this lemma exists in the literature, we have not been able to find it; hence we provide a proof.

Proof of statement (B). Suppose that Condition 3(i) holds. For any $\theta \in \Theta_0$, there exists a collection of closed walks $\{\gamma_i\}_{i=1}^{q}$ connected by paths $\{\theta_i\}_{i=1}^{q+1}$ such that

$$\theta = \theta_1 + \gamma_1 + \theta_2 + \cdots + \gamma_q + \theta_{q+1},$$

where $\gamma_i \in \Xi_{j_i}$ with $j_i \in \{1, \ldots, m_{\text{pro}}\}$ for $i = 1, \ldots, q$ such that $j_i \neq j_{i'}$ for all $i \neq i'$. Then $q \leq m_{\text{pro}}$. As the number of paths in $(\mathcal{V}, \mathcal{E})$ is finite, it suffices to show that the set

$$A_i(x) := \left\{ x + \zeta(\mathfrak{R}(\gamma)) : \gamma \in \Xi_i,\ \text{reac}(\mathfrak{R}(\gamma)) \leq x \right\}$$

is finite for every $x \in \mathbb{N}_0^n$ and $i \in \{1, \ldots, m_{\text{pro}}\}$. For any $i \in \mathcal{C}$, let

$$A_{i,k}(x) = \left\{ x + \zeta(\mathfrak{R}(\gamma)) : \gamma \in \Xi_i,\ x \geq \text{reac}(\mathfrak{R}(\gamma)),\ |\mathcal{C}_\gamma| = k \right\},$$

with $k \in \{1, \ldots, m_{\text{pro}}\}$ and $\mathcal{C}_\gamma = \{U_i \in \mathcal{U} : U_i \in \gamma\}$. Then $A_i(x) = \bigcup_{k=1}^{m_{\text{pro}}} A_{i,k}(x)$ for $i \in \{1, \ldots, m_{\text{pro}}\}$. We aim to show that $A_{i,k}(x)$ is a finite set for all $i \in \{1, \ldots, m_{\text{pro}}\}$, $1 \leq k \leq m_{\text{pro}}$, and $x \in \mathbb{N}_0^n$ by induction on k.

Fix any $i_0 \in \{1, \ldots, m_{\text{pro}}\}$. Note that $\{\Gamma \in \Xi_{i_0} \colon |\mathcal{C}_\gamma| = 1\} = \mathcal{R}_{i_0,i_0}$ is a finite set. Thus, by Condition 3(i) and Lemma 6, $A_{i_0,1}(x)$ is finite. For $k \geq 2$, we show that $A_{i_0,k}(x)$ is finite by contradiction. Suppose that $A_{i_0,k}(x)$ is not a finite set. Then there exists a sequence of closed walks $\{\gamma_j\}_{j\geq 1} \subseteq \Xi_i$ such that the following hold:

(a) $|\mathcal{C}_{\gamma_j}| = k$ and $x \geq \text{reac}(\mathfrak{R}(\gamma_j))$ for all $i \in \mathbb{N}$;

(b) $\{x + \zeta(\mathfrak{R}(\gamma_j))\}_{j\geq 1} \subseteq A_{i,k}$ is an infinite subset of $\mathbb{N}_0^n$;

(c) $\zeta(\mathfrak{R}(\gamma_j)) \neq \zeta(\mathfrak{R}(\gamma_{j'}))$ for all indexes $j \neq j'$.

Using Lemma 5, we can assume that $\{\zeta(\mathfrak{R}(\gamma_j))\}_{j\geq 1}$ is a strictly increasing sequence. Next, for every $j \in \mathbb{N}$, γ_j can be decomposed as $\gamma_j = \gamma_{j,1} + \cdots + \gamma_{j,q_j}$ such that for $j' = 1, \ldots, q_j$, $\gamma_{j,j'} \in \Xi_{i_0}$, and U_{i_0} only appears as the initial and terminal nodes of $\gamma_{j,j'}$. Assume that

$$\sum_{j'=k_1}^{k_2} \zeta\left(\mathfrak{R}(\gamma_{j,j'})\right) \neq 0 \quad \text{for all } 1 \leq k_1 \leq k_2 \leq q_i. \tag{38}$$

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Otherwise, we can replace γ_j by $\gamma_j' = \gamma_{j,1} + \cdots + \gamma_{j,k_1-1} + \gamma_{j,k_2+1}$. Then $\mathrm{reac}(\gamma_j') \le \mathrm{reac}(\gamma_j) \le x$ and $\zeta(\mathfrak{R}(\gamma_j')) = \zeta(\mathfrak{R}(\gamma_j))$. Thus, with this substitution, properties (a)–(c) still hold.

For any $i \in \mathbb{N}$, $\gamma_{i,1}$ can be decomposed into at most $k-1$ closed walks connected by paths. By the induction hypothesis, for any $x \in \mathbb{N}_0^n$, the set $\{x + \zeta(\mathfrak{R}(\gamma_{i,1}))\}_{i\ge1}$ is finite. Thus, for any positive integer q and any index j, $\{x + \zeta(\mathfrak{R}(\gamma_{j,1})) + \cdots + \zeta(\mathfrak{R}(\gamma_{j,j'}))\}_{j'=1}^{q_j \wedge q}$ is a finite set. Therefore, if $\{q_j\}_{j\ge1}$ is finite, then so is $\{x + \zeta(\mathfrak{R}(\gamma_j))\}_{j\ge1}$. This contradicts (b). Thus, by taking subsequences if necessary, we can assume that $\{q_j\}_{j\ge1}$ is a strictly increasing sequence of positive integers. Let

$$\eta_{j,j'} := x + \zeta\left(\mathfrak{R}(\gamma_{j,1})\right) + \cdots + \zeta\left(\mathfrak{R}(\gamma_{j,j'})\right)$$

for all $j \in \mathbb{N}$ and $j' \in \{1, \ldots, q_j\}$. It follows from (a) that $\eta_{j,j'} \in \mathbb{N}_0^n$. Recall that $\{\eta_{j,1}\}_{j\ge1} = \{x + \zeta(\mathfrak{R}(\gamma_{j,1}))\}_{j\ge1}$ is a finite set. There exists a subsequence $\{\eta_{n_j^1,1}\}_{j\ge1}$ of $\{\eta_{j,1}\}_{j\ge1}$ such that $\eta_{n_j^1,1} = y_1 \in \mathbb{N}_0^n$ for all indexes j'. Iteratively, for any $k \ge 2$, there exists a subsequence $\{\eta_{n_j^k,k}\}_{j\ge1}$ of $\{\eta_{n_j^{k-1},k}\}_{j\ge1}$ such that $\eta_{n_j^k,k} = y_k \in \mathbb{N}_0^n$ for all $j \in \mathbb{N}$. Concerning Condition 3(i), the sequence $\{y_k\}_{k\ge1} \subseteq \mathbb{N}_0^n$ satisfies the property that

$$y_k - y_{k'} = \eta_{n_k^k,k} - \eta_{n_k^k,k'} = \sum_{j=k'+1}^{k} \zeta\left(\mathfrak{R}(\gamma_{n_k^k,j})\right) \notin \mathbb{N}_0^n \setminus \{0\} \quad \text{for all } k > k' \ge 1. \tag{39}$$

On the other hand, as a result of assumption (38), we have $y_k \ne y_{k'}$ for all $k \ne k'$. Thus, according to Lemma 5, there exists a strictly increasing subsequence of $\{y_k\}_{k\ge1}$, which contradicts (39). This proves that $A_{i,k}(x)$ is a finite set for all $i \in \{1, \ldots, m_{\mathrm{pro}}\}$ and $1 \le k \le m_{\mathrm{pro}}$. Therefore, $A_i(x) = \bigcup_{k=1}^{m_{\mathrm{pro}}} A_{i,k}(x)$ is also finite, and so is $\mathcal{X}_0$. The proof of statement (B) is complete.

Now it suffices to prove Lemmas 5 and 6. Note that Lemma 5 is elementary, so we only provide the proof of Lemma 6.

Proof of Lemma 6. (i) $\Longrightarrow$ (ii) is straightforward: if (ii) fails, then there exists $\eta \in \mathcal{H} \cap \mathbb{N}_0^n \setminus \{0\}$; this implies that $\mathcal{G} := \{j\eta : j \in \mathbb{N}\}$ is an infinite subset of $\mathcal{H}_x$, which contradicts (i).

Conversely, suppose that (ii) holds. Let $V \subseteq \mathbb{N}_0^q$ be a set such that $\mathcal{H}_{x,V} := \{x + v(\mathcal{Z}) : v \in V\} = \mathcal{H}_x$. By Zorn's lemma, we can assume that V is minimal, namely for any $v \in V$, with $V' = V \setminus \{v\}$ one has that $\mathcal{H}_{x,V'} \ne \mathcal{H}_x$. To prove that H_x is finite, it suffices to show that V is a finite set. Suppose that V is an infinite set. Then there is a sequence $\{v_i\}_{i\ge1} \subseteq V$ such that $v_i \ne v_j$ for any $i \ne j$. Referring to Lemma 5, by taking subsequences, we can assume that $\{v_i\}_{i\ge1}$ is strictly increasing.

For any $\eta \in \mathcal{H}_x$, we have $\eta \ge -x$. Thus, $\{v_i(\mathcal{Z})\}_{i\ge1} \subseteq \mathcal{H}_x$ is bounded from below. Owing to the minimality of V, we have $v_i(\mathcal{Z}) \ne v_j(\mathcal{Z})$ whenever $i \ne j$, and thus by Lemma 5 we assume that $\{v_i(\mathcal{Z})\}_{i\ge1}$ is strictly increasing. Because $\{v_i\}_{i\ge1}$ is strictly increasing, it follows that $v_0 := v_2 - v_1 \in \mathbb{N}_0^{q,*}$ and $v_0(\mathcal{Z}) = v_2(\mathcal{Z}) - v_1(\mathcal{Z}) \in \mathcal{H} \cap \mathbb{N}_0^n \setminus \{0\}$. This contradicts (ii). The proof is complete. □

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Competing Interests

There were no competing interests to declare which arose during the preparation or publication process of this article.

References

[1] ANDERSON, D. F. AND COTTER, S. L. (2016). Product-form stationary distributions for deficiency zero networks with non-mass action kinetics. *Bull. Math. Biol.* **78**(12), 2390–2407.

[2] ANDERSON, D. F., CRACIUN, G. AND KURTZ, T. G. (2010). Product-form stationary distributions for deficiency zero chemical reaction networks. *Bull. Math. Biol.* **72**, 1947–1970.

[3] ANDERSON, D. F. AND KURTZ, T. G. (2015). *Stochastic Analysis of Biochemical Systems*. Mathematical Biosciences Institute Lecture Series. Springer, Cham,

[4] ASMUSSEN, S. (2008). *Applied Probability and Queues*. Stochastic Modelling and Applied Probability. Springer New York.

[5] CAPPELLETTI, D. AND JOSHI, B. (2018). Graphically balanced equilibria and stationary measures of reaction networks. *SIAM J. Appl. Dyn. Syst.* **17**(3), 2146–2175.

[6] CAPPELLETTI, D., and MAJUMDER, A. P. AND WIUF, C. (2021). The dynamics of stochastic mono-molecular reaction systems in stochastic environments. *Stoch. Proc. Appl.* **137**, 106–148.

[7] CAPPELLETTI, D. AND WIUF, C. (2016). Elimination of intermediate species in multiscale stochastic reaction networks. *Ann. Appl. Probab.* **26**(5), 2915–2958.

[8] CAPPELLETTI, D. AND WIUF, C. (2016). Product-form Poisson-like distributions and complex balanced reaction systems. *SIAM J. Appl. Math.* **76**(1), 411–432.

[9] DESHPANDE, A. AND GOPALKRISHNAN, M. (2014). Autocatalysis in reaction networks. *Bull. Math. Biol.* **76**, 2570–2595.

[10] FEINBERG, M. (2019). *Foundations of Chemical Reaction Network Theory*, 1 ed. Applied Mathematical Sciences, Vol. **202**. Springer, Cham.

[11] FELIU, E. AND WIUF, C. (2012). Variable elimination in chemical reaction networks with mass-action kinetics. *SIAM J. Appl. Math.* **72**(4), 959–981.

[12] FELIU, E. AND WIUF, C. (2013). Simplifying biochemical models with intermediate species. *J. R. Soc. Interface* **10**(87).

[13] HOESSLY, H. AND WIUF, C. (2021). Fast reactions with non-interacting species in stochastic reaction networks. *Math. Biosci. Eng.* **19**(3), 2720–2749.

[14] HOESSLY, L., WIUF, C. AND XIA, P. (2023). On the sum of chemical reactions. *Euro. J. Appl. Math.* **34**, 303–325.

[15] HOESSLY, L., WIUF, C. AND XIA, P. (2025) Reaction cleaving and complex-balanced distributions for chemical reaction networks with general kinetics. *Peer Community* J. 5, article no. e87.

[16] HONG, H., HERNANDEZ, B. S., KIM, J. AND KIM, J. K. (2023). Computational translation framework identifies biochemical reaction networks with special topologies and their long-term dynamics. *SIAM J. Appl. Math.* **83**(3), 1025–1048.

[17] HONG, H., KIM, J., AL-RADHAWI, M. A., SONTAG, E. D. AND KIM, J. K. (2021). Derivation of stationary distributions of biochemical reaction networks via structure transformation. *Commun. Biol.* **4**(1), 1–10.

[18] INGALLS, B. (2013). *Mathematical Modeling in Systems Biology*. MIT Press, Cambridge.

[19] KANG, H.-W. AND KURTZ, T. G. (2013). Separation of time-scales and model reduction for stochastic reaction networks. *Ann. Appl. Probab.* **23**(2), 529–583.

[20] KURTZ, T. G. (1972). The relationship between stochastic and deterministic models for chemical reactions. *J. Chem. Phys.* **57**, 2976–2978.

[21] MARCONDES DE FREITAS, M., FELIU, E. AND WIUF, C. (2017). Intermediates, catalysts, persistence, and boundary steady states. *J. Math. Biol.* **74**, 887–932.

[22] MCQUARRIE, D. (1967). Stochastic approach to chemical kinetics. *J. Appl. Probab.* **85**, 413–478.

[23] NORRIS, J. R. (1997). *Markov Chains*. Cambridge University Press, Cambridge.

[24] PECCOUD, J. AND YCART, B. (1995). Markovian modelling of gene product synthesis. *Theor. Pop. Biol.* **48**(2), 222–234.

[25] PFAFFELHUBER, P. AND POPOVIC, L. (2015). Scaling limits of spatial compartment models for chemical reaction networks. *Ann. Appl. Probab.* **25**(6), 3162–3208.

[26] R Core Team (2025). *R: A Language and Environment for Statistical Computing*. R Foundation for Statistical Computing, Vienna, Austria. URL: https://www.R-project.org/.

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[27] SÁEZ, M., WIUF, C. AND FELIU, E. (2017). Graphical reduction of reaction networks by linear elimination of species. *J. Math. Biol.* **74**(1), 195–237.
[28] WICKHAM, H. (2016) *ggplot2: Elegant Graphics for Data Analysis*. Springer-Verlag, New York. ISBN 978-3-319-24277-4.

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