

SOME NETWORK CONDITIONS FOR POSITIVE RECURRENCE OF STOCHASTICALLY MODELED REACTION NETWORKS*

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Abstract. We consider discrete-space continuous-time Markov models of reaction networks and provide sufficient conditions for the following stability condition to hold: each state in a closed, irreducible component of the state space is positive recurrent; moreover the time required for a trajectory to enter such a component has finite expectation. The provided analytical results depend solely on the underlying structure of the reaction network and not on the specific choice of model parameters. Our main results apply to binary systems, and our main analytical tool is the “tier structure” previously utilized successfully in the study of deterministic models of reaction networks.

Key words. stochastic reaction networks, positive recurrence, continuous-time Markov chain, Foster–Lyapunov criteria

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1. Introduction. Mathematical models of reaction networks generally fall into two categories. When the counts of the constituent species are high a (usually non-linear) set of ordinary differential equations is used to model their concentrations. However, when the abundances are low a continuous-time Markov chain is often used to model the counts of the different species. In this paper we consider the stochastic model and provide conditions on the associated reaction network that ensure the Markov chain satisfies the following: each state in a closed, irreducible component of the state space is positive recurrent; moreover, if τ_{x_0} is the time for the process to enter the union of the closed irreducible components given an initial condition x_0 , then $\mathbb{E}[\tau_{x_0}] < \infty$. Note, therefore, that even if the initial condition of the process is a transient state, the trajectory will eventually enter a positive recurrent component of the state space. Importantly, the main analytical results provided here hold regardless of the choice of rate parameters for the model, which are often unknown.

This work falls into the broad research area known as chemical reaction network theory, which dates back to at least [31, 32], where graphical characteristics of networks were shown to ensure uniqueness and local asymptotic stability of the steady states for deterministically modeled complex-balanced systems. Since that time, much of the focus of chemical reaction network theory has been related to discovering how the qualitative properties of deterministic models relate to their reaction networks [3, 4, 8, 10, 12, 14, 17, 18, 21, 22, 23, 24, 29, 34, 38, 39]. However, with the advent of new technologies—most notably fluorescent proteins—there is now a large literature demonstrating that the fluctuations arising from the effective randomness of individual interactions in cellular systems can have significant consequences on the emergent behavior of the system [9, 11, 19, 33, 36, 40, 41]. Hence, analytical results

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related to stochastic models are essential if these systems are to be well understood, and attention is shifting in their direction.

In the deterministic modeling regime there are a number of network conditions that guarantee some sort of stability for the model. These conditions include weak reversibility and deficiency zero [21, 22, 23], weak reversibility and a single linkage class [3, 4], endotactic [18], strongly endotactic [29], tropically endotactic [13], etc. However, to the best of the authors’ knowledge, in the stochastic context there is only one such result: in [5] a model whose reaction network is weakly reversible and has a deficiency of zero is shown to be positive recurrent (and the stationary distribution is characterized as a product of Poisson distributions). (The paper [30] provides sufficient conditions for positive recurrence, but the provided conditions are analytical in nature and do not explicitly relate to the network structure of the model.) Here we provide network conditions guaranteeing stability for two classes of binary models: (i) models that are weakly reversible, have a single linkage class, and have in-flows and out-flows, and (ii) a new category of networks we term “double-full.” We will show that all states are positive recurrent for the first class of models. We will show that for the second class of models the stability condition detailed in the opening paragraph holds: all states in closed, irreducible components of the state space are positive recurrent, and every trajectory enters such a component in finite time. Our main analytic tools are Lyapunov functions and ideas related to “tier structures” as introduced in [3, 4] and also utilized in [29].

The outline of this paper is as follows. In section 2, we introduce the relevant mathematical model, including the required terminology from chemical reaction network theory, and provide a statement of the main results. In section 3, we generalize the “tier structure” developed in [3, 4] and present some preliminary analytical results. In section 4, we provide a general result relating the tiers of a reaction network to the stability of the Markov model. In section 5, we restate our main results and provide their proofs. We also introduce some generalizations of our main results. Finally, in section 6, we provide a brief discussion and directions for future research. In particular, we discuss how we believe weak reversibility alone guarantees positive recurrence, and that this conjecture, which is similar to the global attractor conjecture for deterministically modeled systems, will be an active area of future research.

2. Mathematical model and a statement of the main results. In section 2.1, we formally introduce reaction networks. In section 2.2, we introduce both the deterministic and stochastic models. In section 2.3, we state our main results.

2.1. Reaction networks. A reaction network is a graphical construct that describes the set of possible interactions among the constituent species.

DEFINITION 1. A reaction network is given by a triple of finite sets $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ where the following apply:

1. The species set $\mathcal{S} = \{S_1, S_2, \dots, S_d\}$ contains the species of the reaction network.
2. The reaction set $\mathcal{R} = \{R_1, R_2, \dots, R_r\}$ consists of ordered pairs $(y, y') \in \mathcal{R}$ where

$$(1) \quad y = \sum_{i=1}^d y_i S_i \quad \text{and} \quad y' = \sum_{i=1}^d y'_i S_i$$

and where the values $y_i, y'_i \in \mathbb{Z}_{\geq 0}$ are the stoichiometric coefficients. We will often write reactions (y, y') as $y \rightarrow y'$.

3. The complex set \mathcal{C} consists of the linear combinations of the species in (1). Specifically, $\mathcal{C} = \{y \mid y \rightarrow y' \in \mathcal{R}\} \cup \{y' \mid y \rightarrow y' \in \mathcal{R}\}$. For the reaction $y \rightarrow y'$, the complexes y and y' are termed the source and product complex of the reaction, respectively.

Allowing for a slight abuse of notation, we will let y denote both the linear combination in (1) and the vector whose i th component is y_i , i.e., $y = (y_1, y_2, \dots, y_d)^T \in \mathbb{Z}_{\geq 0}^d$. For example, when $\mathcal{S} = \{S_1, S_2, \dots, S_d\}$, $2S_1 + S_2$ is associated with $(2, 1, 0, \dots, 0) \in \mathbb{Z}_{\geq 0}^d$.

Note that it is perfectly valid to have a linear combination of the form (1) with $y_i = 0$ for each i . In this case, we denote the complex by \emptyset .

It is most common to present a reaction network with a directed *reaction graph* in which the nodes are the complexes and the directed edges are given by the reactions. We present an example to solidify notation.

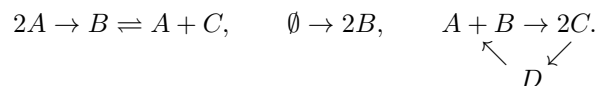
Example 1. Consider the reaction network with associated reaction graph



which is a usual model for substrate-enzyme kinetics. For this reaction network, $\mathcal{S} = \{S, E, SE, P\}$, $\mathcal{C} = \{S + E, SE, E + P\}$, and $\mathcal{R} = \{S + E \rightarrow SE, SE \rightarrow S + E, SE \rightarrow E + P\}$.

DEFINITION 2. Let $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ be a reaction network. The connected components of the associated reaction graph are termed linkage classes. If a linkage class is strongly connected, then it is called weakly reversible. If all linkage classes in a reaction network are weakly reversible, then the reaction network is said to be weakly reversible.

Example 2. Consider the reaction network with associated reaction graph



This network has three linkage classes. The rightmost linkage class is weakly reversible, whereas the other two are not.

We will denote by $\mathcal{S}(\mathcal{L})$, $\mathcal{C}(\mathcal{L})$, and $\mathcal{R}(\mathcal{L})$ the sets of species, complexes, and reactions involved in linkage class \mathcal{L} , respectively.

The following definitions related to possible network structures are required to state our main results.

DEFINITION 3. A reaction network $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ is called binary if $\sum_{i=1}^d y_i \leq 2$ for all $y \in \mathcal{C}$.

DEFINITION 4. Let $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ be a reaction network with $\mathcal{S} = \{S_1, S_2, \dots, S_d\}$. The complex \emptyset is termed the zero complex. Complexes of the form S_i are termed unary complexes, and complexes of the form $S_i + S_j$ are termed binary complexes. Binary complexes of the form $2S_i$ are termed double complexes. If $2S_i \in \mathcal{C}$ for each $i = 1, 2, \dots, d$, then the reaction network $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ is double-full.

DEFINITION 5. We call the reactions $\emptyset \rightarrow S$ and $S \rightarrow \emptyset$ the in-flow and out-flow of S , respectively. We say a reaction network has all in-flows and out-flows if $\emptyset \rightarrow S \in \mathcal{R}$ and $S \rightarrow \emptyset \in \mathcal{R}$ for each $S \in \mathcal{S}$.

2.2. Dynamical systems. In this section, we introduce two dynamical models for reaction networks. We begin with the usual Markov chain model and then present the deterministic model.

For the usual Markov model the vector $X(t) \in \mathbb{Z}_{\geq 0}^d$ gives the counts of the constituent species at time t , and the transitions are determined by the reactions. In particular, for appropriate state-dependent intensity (or rate) functions $\lambda_{y \rightarrow y'} : \mathbb{Z}_{\geq 0}^d \rightarrow \mathbb{R}_{\geq 0}$ we assume that for each $y \rightarrow y' \in \mathcal{R}$,

$$(2) \quad P(X(t + \Delta t) = x + y' - y \mid X(t) = x) = \lambda_{y \rightarrow y'}(x)\Delta t + o(\Delta t).$$

The generator \mathcal{A} of the associated Markov process is [20]

$$(3) \quad \mathcal{A}V(x) = \sum_{y \rightarrow y' \in \mathcal{R}} \lambda_{y \rightarrow y'}(x)(V(x + y' - y) - V(x))$$

for a function $V : \mathbb{Z}_{\geq 0}^d \rightarrow \mathbb{R}$. The usual choice of intensity is given by *stochastic mass-action kinetics*

$$(4) \quad \lambda_{y \rightarrow y'}(x) = \kappa_{y \rightarrow y'} \prod_{i=1}^d \frac{x_i!}{(x_i - y_i)!} \mathbf{1}_{\{x_i \geq y_i\}},$$

where the positive constant $\kappa_{y \rightarrow y'}$ is the reaction rate constant. We typically incorporate the rate constants into the reaction graphs by placing them next to the reaction arrow as in $y \xrightarrow{\kappa} y'$. Trajectories of this model are typically simulated via the Gillespie algorithm [26, 27] or the next reaction method [1, 25] or are approximated via tau-leaping [2, 28].

For the deterministic model, we let the vector $x(t) \in \mathbb{R}_{\geq 0}^d$ solve

$$(5) \quad \frac{d}{dt}x(t) = \sum_{y \rightarrow y'} \kappa_{y \rightarrow y'} x(t)^y (y' - y),$$

where for two vectors $u, v \in \mathbb{R}_{\geq 0}^d$, we define $u^v = \prod_{i=1}^d u_i^{v_i}$ with the convention $0^0 = 1$. The vector $x(t)$ then models the concentrations of the constituent species at time t . See [6, 7, 35] for the connection between the stochastic and deterministic models. The choice of rate function, i.e., $\kappa_{y \rightarrow y'} x(t)^y$, is termed *deterministic mass-action kinetics*.

Recalling the discussion below Definition 1, we will sometimes write $x^{\sum_{i=1}^d y_i S_i}$ for $\prod_{i=1}^d x_i^{y_i}$. For example, we have $x^{2S_1 + S_2} = x_1^2 x_2$.

2.3. Statement of main results. In this section we state our main results. The first, Theorem 1, is similar to the main results found in [3, 4] related to deterministic systems that are weakly reversible and have a single linkage class.

THEOREM 1. *Let $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ be a weakly reversible, binary reaction network that has a single linkage class. Let $\tilde{\mathcal{R}} = \mathcal{R} \cup_{S \in \mathcal{S}} \{\emptyset \rightarrow S, S \rightarrow \emptyset\}$ and $\tilde{\mathcal{C}} = \mathcal{C} \cup \{\emptyset\} \cup \{S \mid S \in \mathcal{S}\}$. Then, for any choice of rate constants, every state of the Markov process with intensity functions (4) associated to the reaction network $(\mathcal{S}, \tilde{\mathcal{C}}, \tilde{\mathcal{R}})$ is positive recurrent.*

Our second main result is related to models that are double-full.

THEOREM 2. *Let $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ be a binary reaction network satisfying the following two conditions:*

1. the reaction network is double-full, and
2. for each double complex (of the form $2S_i$) there is a directed path within the reaction graph beginning with the double complex itself and ending with either a unary complex (of the form S_j) or the zero complex.

Then, for any choice of rate constants, the Markov process with intensity functions (4) associated to the reaction network $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ satisfies the following: each state in a closed, irreducible component of the state space is positive recurrent; moreover, if τ_{x_0} is the time for the process to enter the union of the closed irreducible components given an initial condition x_0 , then $\mathbb{E}[\tau_{x_0}] < \infty$.

3. Mathematical preliminaries: Lyapunov functions and tiers. In this section we introduce the well-known Foster–Lyapunov conditions. We also generalize the “tier structure” that was introduced in [3, 4] for continuous, deterministic models to the discrete, stochastic setting. In section 4, we will use the new ideas related to tiers to ensure the Foster–Lyapunov conditions hold for our models of interest.

The theorem below relating Lyapunov functions with positive recurrence of a Markov model is well known. See [37] for more on this topic.

THEOREM 3. *Let X be a continuous-time Markov chain on a countable state space \mathbb{S} with generator \mathcal{A} . Suppose there exists a finite set $K \subset \mathbb{S}$ and a positive function V on \mathbb{S} such that*

$$(6) \quad \mathcal{A}V(x) \leq -1$$

for all $x \in \mathbb{S} \setminus K$. Then each state in a closed, irreducible component of \mathbb{S} is positive recurrent. Moreover, if τ_{x_0} is the time for the process to enter the union of the closed irreducible components given an initial condition x_0 , then $\mathbb{E}[\tau_{x_0}] < \infty$.

In this paper, our main Lyapunov function will be $V(x) = \sum_{i=1}^d v(x_i)$, where

$$(7) \quad v(x) = \begin{cases} x(\ln x - 1) + 1 & \text{if } x \in \mathbb{Z}_{\geq 0} \\ 1, & \text{otherwise} \end{cases}$$

with the convention $0 \ln 0 = 0$. This function has been used widely to verify the stability of deterministic models of reaction networks. In particular, it played a significant role in the proof of the deficiency zero theorem of chemical reaction network theory [21, 22, 23, 32].

We turn to the task of generalizing the tier structures introduced in [3, 4] to the discrete state space setting. The key difference between the present setting and that of [3, 4] is that now the process can hit the boundary of the state space, where intensity functions can take the value of zero.

We begin by introducing some useful terminology.

1. For $x \in \mathbb{Z}^d$, we write $(x \vee 1)$ for the vector in \mathbb{Z}^d with j th component $(x \vee 1)_j = x_j \vee 1 = \max\{x_j, 1\}$.
2. We will use the phrase “for large n ” for “for all n greater than some fixed constant N .”
3. For each complex $y \in \mathcal{C}$, we define the following function,

$$\lambda_y(x) := \prod_{i=1}^d \frac{x_i!}{(x_i - y_i)!} \mathbf{1}_{\{x_i \geq y_i\}} \quad \text{for } x \in \mathbb{Z}^d.$$

Note that for the reaction $y \rightarrow y' \in \mathcal{R}$, we have $\lambda_{y \rightarrow y'}(x) = \kappa_{y \rightarrow y'} \lambda_y(x)$. That is, $\lambda_y(x)$ is the portion of the stochastic mass-action term that depends upon the source complex y .

We now define two types of tiers: D-type and S-type. The D-type and S-type tiers will allow us to later quantify the relative sizes of the different terms in the expression for \mathcal{AV} , where V is defined in and around (7), required to utilize Theorem 3. In particular, you can see in (8) the precise functional role each term plays in \mathcal{AV} .

DEFINITION 6. Let $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ be a reaction network, and let $\{x_n\}$ be a sequence in $\mathbb{R}_{\geq 0}^d$. We say that \mathcal{C} has a D-type partition along $\{x_n\}$ if there exist a finite number of nonempty mutually disjoint subsets $T_{\{x_n\}}^{D,i} \subset \mathcal{C}$ such that $\cup_i T_{\{x_n\}}^{D,i} = \mathcal{C}$ and

1. if $y, y' \in T_{\{x_n\}}^{D,i}$, then there exists a $C \in (0, \infty)$ such that

$$\lim_{n \rightarrow \infty} \frac{(x_n \vee 1)^y}{(x_n \vee 1)^{y'}} = C,$$

2. if $y \in T_{\{x_n\}}^{D,i}$ and $y' \in T_{\{x_n\}}^{D,k}$ with $i < k$, then

$$\lim_{n \rightarrow \infty} \frac{(x_n \vee 1)^{y'}}{(x_n \vee 1)^y} = 0.$$

The mutually disjoint subsets $T_{\{x_n\}}^{D,i}$ are called D-type tiers along $\{x_n\}$. We will say that y is in a higher tier than y' in the D-type partition along $\{x_n\}$ if $y \in T_{\{x_n\}}^{D,i}$ and $y' \in T_{\{x_n\}}^{D,j}$ with $i < j$. In this case, we will denote $y \succ_D y'$. If y and y' are in the same D-type tier, then we will denote this by $y \sim_D y'$.

Note that \mathcal{C} is a well-ordered set with \succ_D and \sim_D .

The terminology of saying tier $T_{\{x_n\}}^{D,1}$ is higher than the other tiers comes from point 2 in Definition 6.

DEFINITION 7. Let $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ be a reaction network, and let $\{x_n\}$ be a sequence in $\mathbb{R}_{\geq 0}^d$. We say that \mathcal{C} has a S-type partition along $\{x_n\}$ if there exist a finite number of nonempty mutually disjoint subsets $T_{\{x_n\}}^{S,i} \subset \mathcal{C}$ with $i \in \{1, \dots, P, \infty\}$ such that $T_{\{x_n\}}^{S,1} \cup \dots \cup T_{\{x_n\}}^{S,P} \cup T_{\{x_n\}}^{S,\infty} = \mathcal{C}$ and

1. $y \in T_{\{x_n\}}^{S,\infty}$ if and only if $\lambda_y(x_n) = 0$ for all n ,
2. $\lambda_y(x_n) \neq 0$ for any n if $y \in T_{\{x_n\}}^{S,i}$ for $i \in \{1, \dots, P\}$,
3. if $y, y' \in T_{\{x_n\}}^{S,i}$, with $i \in \{1, \dots, P\}$, then there exists a $C \in (0, \infty)$ such that

$$\lim_{n \rightarrow \infty} \frac{\lambda_y(x_n)}{\lambda_{y'}(x_n)} = C,$$

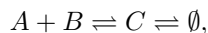
4. if $y \in T_{\{x_n\}}^{S,i}$ and $y' \in T_{\{x_n\}}^{S,k}$ with $1 \leq i < k \leq P$, then

$$\lim_{n \rightarrow \infty} \frac{\lambda_{y'}(x_n)}{\lambda_y(x_n)} = 0.$$

The mutually disjoint subsets $T_{\{x_n\}}^{S,i}$ are called S-type tiers along $\{x_n\}$. We will say that y is in a higher tier than y' in the S-type partition along $\{x_n\}$ if $y \in T_{\{x_n\}}^{S,i}$ and $y' \in T_{\{x_n\}}^{S,j}$ with $i < j$.

We present an example in order to clarify the previous two definitions.

Example 3. Consider the reaction network



and let $x_n = (n^2, 0, n)$. For this sequence and this reaction network we have

$$(x_n \vee 1)^{A+B} = n^2, \quad (x_n \vee 1)^C = n, \quad \text{and} \quad (x_n \vee 1)^\emptyset = 1,$$

and so

$$T_{\{x_n\}}^{D,1} = \{A + B\}, \quad T_{\{x_n\}}^{D,2} = \{C\}, \quad T_{\{x_n\}}^{D,3} = \{\emptyset\}.$$

However,

$$\lambda_{A+B}(x_n) = 0, \quad \lambda_C(x_n) = n, \quad \text{and} \quad \lambda_\emptyset(x_n) = 1,$$

so that

$$T_{\{x_n\}}^{S,\infty} = \{A + B\}, \quad T_{\{x_n\}}^{S,1} = \{C\}, \quad T_{\{x_n\}}^{S,2} = \{\emptyset\}.$$

These two tier structures make hierarchies for the complexes with respect to the sizes of $(x_n \vee 1)^y$ and $\lambda_y(x_n)$ along a sequence $\{x_n\}$.

DEFINITION 8. Let $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ be a reaction network, and suppose that $\{T_{\{x_n\}}^{D,i}\}$ are D -type tiers along a sequence $\{x_n\}$. We will call $y \rightarrow y' \in \mathcal{R}$ a descending reaction along $\{x_n\}$ if $y \in T_{\{x_n\}}^{D,1}$ and $y' \in T_{\{x_n\}}^{D,i}$ for some $i > 1$. We denote

$$D_{\{x_n\}} := \{y \in \mathcal{C} \mid y \rightarrow y' \text{ is a descending reaction along } \{x_n\}\}.$$

For example, note that for the reaction network and sequence of Example 3, the set of descending reactions along $\{x_n\}$ is $\{A + B \rightarrow C\}$ and so $D_{\{x_n\}} = \{A + B\}$.

DEFINITION 9. For a network $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ with $|\mathcal{S}| = d$, a sequence $\{x_n\} \subset \mathbb{Z}_{\geq 0}^d$ is called a tier-sequence if

1. $\lim_{n \rightarrow \infty} x_{n,i} \in [0, \infty]$ for all $i = 1, 2, \dots, d$ and $\lim_{n \rightarrow \infty} x_{n,i} = \infty$ for at least one i , and
2. \mathcal{C} has both a D -type partition and an S -type partition along $\{x_n\}$.

Note that $\{x_n\}$ given in Example 3 is a tier-sequence for the given reaction network.

LEMMA 4. Let $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ be a reaction network with $|\mathcal{S}| = d$, and let $\{x_n\} \subset \mathbb{Z}_{\geq 0}^d$ be an arbitrary sequence such that $\lim_{n \rightarrow \infty} |x_n| = \infty$. Then there exists a subsequence of $\{x_n\}$ which is a tier-sequence.

The proof of Lemma 4 is similar to that of Lemma 4.2 in [3]. In particular, the relevant tiers can each be constructed sequentially by repeatedly taking subsequences. The details are omitted for the sake of brevity.

LEMMA 5. Let $\{x_n\}$ be a tier-sequence of a reaction network $(\mathcal{S}, \mathcal{C}, \mathcal{R})$. If $y_0 \in T_{\{x_n\}}^{D,1}$, then $\lim_{n \rightarrow \infty} (x_n \vee 1)^{y_0} = \infty$.

Proof. Let $I = \{i \mid \lim_{n \rightarrow \infty} x_{n,i} = \infty\}$ and $y \in \mathcal{C}$ such that $y_i \neq 0$ for some $i \in I$. By definition, if $y_0 \in T_{\{x_n\}}^{D,1}$, then

$$\lim_{n \rightarrow \infty} \frac{(x_n \vee 1)^y}{(x_n \vee 1)^{y_0}} = C$$

for some constant $C \geq 0$. Since $\lim_{n \rightarrow \infty} (x_n \vee 1)^y = \infty$, the result follows. \square

In the next lemma, we provide relations between D-type partitions and S-type partitions.

LEMMA 6. *Let $\{x_n\}$ be a tier-sequence of a reaction network $(\mathcal{S}, \mathcal{C}, \mathcal{R})$, and let $y \in \mathcal{C}$. Then*

$$\lim_{n \rightarrow \infty} \frac{\lambda_y(x_n)}{(x_n \vee 1)^y} = \begin{cases} 0 & \text{if } y \in T_{\{x_n\}}^{S,\infty}, \\ 1 & \text{if } y \notin T_{\{x_n\}}^{S,\infty}. \end{cases}$$

Proof. If $y \in T_{\{x_n\}}^{S,\infty}$, then $\lambda_y(x_n) = 0$ for all n . If $y \notin T_{\{x_n\}}^{S,\infty}$, then $\lambda_y(x_n)$ and $(x_n \vee 1)^y$ are polynomials with the same degree and the same leading coefficient (of 1). \square

The following corollary is used throughout.

COROLLARY 7. *Let $\{x_n\}$ be a tier-sequence of a reaction network $(\mathcal{S}, \mathcal{C}, \mathcal{R})$. Suppose $y \notin T_{\{x_n\}}^{S,\infty}$ and $y \in T_{\{x_n\}}^{D,1}$. Then $y \in T_{\{x_n\}}^{S,1}$ and $\lim_{n \rightarrow \infty} \lambda_y(x_n) = \infty$.*

Proof. Let $y' \notin T_{\{x_n\}}^{S,\infty}$. Note that

$$\frac{\lambda_{y'}(x_n)}{\lambda_y(x_n)} = \frac{\lambda_{y'}(x_n)}{(x_n \vee 1)^{y'}} \cdot \frac{(x_n \vee 1)^{y'}}{(x_n \vee 1)^y} \cdot \frac{(x_n \vee 1)^y}{\lambda_y(x_n)}.$$

By Lemma 6, as $n \rightarrow \infty$ the first and third terms on the right of the above equation converge to 1. Therefore,

$$\lim_{n \rightarrow \infty} \frac{\lambda_{y'}(x_n)}{\lambda_y(x_n)} = \lim_{n \rightarrow \infty} \frac{(x_n \vee 1)^{y'}}{(x_n \vee 1)^y}.$$

Because $y \in T_{\{x_n\}}^{D,1}$, the last limit is either 0 (if $y' \notin T_{\{x_n\}}^{D,1}$) or some $C > 0$ (if $y' \in T_{\{x_n\}}^{D,1}$). Thus, y' cannot be in a higher tier than y in the S-type partition. Hence, $y \in T_{\{x_n\}}^{S,1}$. Moreover, since $y \notin T_{\{x_n\}}^{S,\infty}$, by Lemma 5 and Lemma 6, we have $\lim_{n \rightarrow \infty} \lambda_y(x_n) = \infty$. \square

4. Tier structures for positive recurrence. In this section, we provide a theorem that provides sufficient conditions on D-type and S-type tiers for the Markov process associated to a reaction network to be stable in the sense of Theorem 3. We require the following lemma.

LEMMA 8. *Let \mathcal{A} be the generator (3) of the continuous-time Markov chain associated to a reaction network $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ with mass-action kinetics (4) and rate constants $\kappa_{y \rightarrow y'}$. Let V be the function defined in and around (7). For each tier-sequence $\{x_n\}$ there is a constant $C > 0$ for which*

$$(8) \quad \mathcal{A}V(x_n) \leq \sum_{y \rightarrow y' \in \mathcal{R}} \kappa_{y \rightarrow y'} \lambda_y(x_n) \left(\ln \left(\frac{(x_n \vee 1)^{y'}}{(x_n \vee 1)^y} \right) + C \right).$$

Proof. Let $I = \{i \mid x_{n,i} \rightarrow \infty \text{ as } n \rightarrow \infty\} \neq \emptyset$. Then for a reaction $y \rightarrow y' \in \mathcal{R}$, there exists $C_{y \rightarrow y'} > 0$ such that

$$\begin{aligned} &V(x_n + y' - y) - V(x_n) \\ &\leq \sum_{i \in I} [(x_{n,i} + y'_i - y_i)(\ln(x_{n,i} + y'_i - y_i) - 1) - x_{n,i}(\ln(x_{n,i}) - 1)] + C_{y \rightarrow y'} \\ &= \sum_{i \in I} [x_{n,i} \ln\left(1 + \frac{y'_i - y_i}{x_{n,i}}\right) + y_i - y'_i + (y'_i - y_i) \ln(x_{n,i} + y'_i - y_i)] + C_{y \rightarrow y'}, \end{aligned}$$

where we simply grouped those terms not going to infinity into the constant. Using the fact that $\lim_{t \rightarrow \infty} (1 + \frac{\alpha}{t})^t = e^\alpha$ for any α , we have that

$$x_{n,i} \ln\left(1 + \frac{y'_i - y_i}{x_{n,i}}\right) + y_i - y'_i \rightarrow 0 \text{ as } n \rightarrow \infty$$

for each $i \in I$. Hence, there are $C'_{y \rightarrow y'} > 0$ for which

$$V(x_n + y' - y) - V(x_n) \leq \sum_{i \in I} (y'_i - y_i) \ln(x_{n,i} + y'_i - y_i) + C'_{y \rightarrow y'}$$

for each n . For each $i \in I$

$$\ln(x_{n,i} + y'_i - y_i)^{y'_i - y_i} - \ln(x_{n,i}^{y'_i - y_i}) \rightarrow 0,$$

as $n \rightarrow \infty$. Thus, there are $C''_{y \rightarrow y'} > 0$ and $C'''_{y \rightarrow y'} > 0$ for which

$$\begin{aligned} V(x_n + y' - y) - V(x_n) &\leq \sum_{i \in I} \ln(x_{n,i}^{y'_i - y_i}) + C''_{y \rightarrow y'} = \ln\left(\prod_{i \in I} \frac{x_{n,i}^{y'_i}}{x_{n,i}^{y_i}}\right) + C''_{y \rightarrow y'} \\ &\leq \ln\left(\prod_{i=1}^d \frac{(x_{n,i} \vee 1)^{y'_i}}{(x_{n,i} \vee 1)^{y_i}}\right) + C'''_{y \rightarrow y'} = \ln\left(\frac{(x_n \vee 1)^{y'}}{(x_n \vee 1)^y}\right) + C'''_{y \rightarrow y'}. \end{aligned}$$

Hence,

$$\begin{aligned} AV(x_n) &= \sum_{y \rightarrow y' \in \mathcal{R}} \kappa_{y \rightarrow y'} \lambda_y(x_n) (V(x_n + y' - y) - V(x_n)) \\ &\leq \sum_{y \rightarrow y' \in \mathcal{R}} \kappa_{y \rightarrow y'} \lambda_y(x_n) \left(\ln\left(\frac{(x_n \vee 1)^{y'}}{(x_n \vee 1)^y}\right) + C'''_{y \rightarrow y'} \right). \end{aligned}$$

The proof is completed by taking $C = \max_{y \rightarrow y' \in \mathcal{R}} \{C'''_{y \rightarrow y'}\}$. □

The following is our main analytic theorem related to tiers.

THEOREM 9. *Let $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ be a reaction network. Suppose that*

$$(9) \quad T_{\{x_n\}}^{S,1} \cap D_{\{x_n\}} \neq \emptyset$$

for any tier-sequence $\{x_n\}$, where $T_{\{x_n\}}^{S,i}$ are the S -type tiers and $D_{\{x_n\}}$ is the set of source complexes for the descending reactions along $\{x_n\}$. Then for any choice of rate

constants the Markov process with intensity functions (4) associated to the reaction network $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ satisfies the following: each state in a closed, irreducible component of the state space is positive recurrent; moreover, if τ_{x_0} is the time for the process to enter the union of the closed irreducible components given an initial condition x_0 , then $\mathbb{E}[\tau_{x_0}] < \infty$.

Proof. We will show there exists a finite set $K \subset \mathbb{Z}_{\geq 0}^d$ such that $\mathcal{A}V(x) \leq -1$ for all $x \in K^c$. An application of Theorem 3 then completes the proof. We proceed with an argument by contradiction. For ease of notation, the positive constant C appearing in different lines may vary.

Suppose, in order to find a contradiction, that there exists a sequence $\{x_n\}$ with $\lim_{n \rightarrow \infty} |x_n| = \infty$ and $\mathcal{A}V(x_n) > -1$ for all n . By Lemma 4, there exists a subsequence which is a tier-sequence. For simplicity, we also denote this tier-sequence by $\{x_n\}$. Denote the S-type tiers, D-type tiers, and source complexes for the descending reactions for this particular tier-sequence by $T_{\{x_n\}}^{S,i}$, $T_{\{x_n\}}^{D,i}$, and $D_{\{x_n\}}$, respectively. Our main hypothesis (9) implies that there exists a reaction $y_0 \rightarrow y'_0$ such that $y_0 \in T_{\{x_n\}}^{D,1} \cap T_{\{x_n\}}^{S,1}$ and $y'_0 \in T_{\{x_n\}}^{D,i}$ for some $i > 1$. Starting with an application of Lemma 8, we have the existence of $C > 0$ for which

$$\begin{aligned}
 \mathcal{A}V(x_n) &\leq \sum_{y \rightarrow y' \in \mathcal{R}} \kappa_{y \rightarrow y'} \lambda_y(x_n) \left(\ln \left(\frac{(x_n \vee 1)^{y'}}{(x_n \vee 1)^y} \right) + C \right) \\
 &= \lambda_{y_0}(x_n) \underbrace{\left(\sum_{\substack{y \rightarrow y' \in \mathcal{R} \\ y' \succ_D y}} \frac{\kappa_{y \rightarrow y'} \lambda_y(x_n)}{\lambda_{y_0}(x_n)} \ln \left(\frac{(x_n \vee 1)^{y'}}{(x_n \vee 1)^y} \right) \right)}_I \\
 &\quad + \underbrace{\sum_{\substack{y \rightarrow y' \in \mathcal{R} \\ y \succ_D y'}} \frac{\kappa_{y \rightarrow y'} \lambda_y(x_n)}{\lambda_{y_0}(x_n)} \ln \left(\frac{(x_n \vee 1)^{y'}}{(x_n \vee 1)^y} \right)}_{II} \\
 (10) \quad &\quad + \underbrace{\sum_{\substack{y \rightarrow y' \in \mathcal{R} \\ y \sim_D y'}} \frac{\kappa_{y \rightarrow y'} \lambda_y(x_n)}{\lambda_{y_0}(x_n)} \ln \left(\frac{(x_n \vee 1)^{y'}}{(x_n \vee 1)^y} \right)}_{III} + \underbrace{\sum_{y \rightarrow y' \in \mathcal{R}} \frac{\kappa_{y \rightarrow y'} \lambda_y(x_n)}{\lambda_{y_0}(x_n)} C}_{IV}.
 \end{aligned}$$

First note that by Corollary 7, we know $\lambda_{y_0}(x_n) \rightarrow \infty$ as $n \rightarrow \infty$. To conclude the proof, we will show that term II will converge to $-\infty$ as $n \rightarrow \infty$ and that all the other terms remain uniformly bounded in n . One fact we will use repeatedly is the following: because $y_0 \in T_{\{x_n\}}^{D,1} \cap T_{\{x_n\}}^{S,1}$, there exists a constant $C' > 0$ such that for all complexes $y \in \mathcal{C}$ and all n large enough

$$(11) \quad \frac{\lambda_y(x_n)}{\lambda_{y_0}(x_n)} < C' \quad \text{and} \quad \frac{(x_n \vee 1)^y}{(x_n \vee 1)^{y_0}} < C'.$$

Note that (11) immediately implies that terms III and IV are uniformly bounded in n .

We turn to term I. By adding and subtracting appropriate log terms,

$$\begin{aligned}
 \text{I} &= \sum_{\substack{y \rightarrow y' \in \mathcal{R} \\ y' \succ_D y}} \frac{\kappa_{y \rightarrow y'} \lambda_y(x_n)}{\lambda_{y_0}(x_n)} \ln \left(\frac{(x_n \vee 1)^{y_0}}{(x_n \vee 1)^y} \right) + \sum_{\substack{y \rightarrow y' \in \mathcal{R} \\ y' \succ_D y}} \frac{\kappa_{y \rightarrow y'} \lambda_y(x_n)}{\lambda_{y_0}(x_n)} \ln \left(\frac{(x_n \vee 1)^{y'}}{(x_n \vee 1)^{y_0}} \right) \\
 (12)
 \end{aligned}$$

$$\begin{aligned}
 &= \sum_{\substack{y \rightarrow y' \in \mathcal{R} \\ y' \succ_D y}} \left(\frac{\kappa_{y \rightarrow y'} \lambda_y(x_n)}{\lambda_{y_0}(x_n)} \frac{(x_n \vee 1)^{y_0}}{(x_n \vee 1)^y} \right) \frac{(x_n \vee 1)^y}{(x_n \vee 1)^{y_0}} \ln \left(\frac{(x_n \vee 1)^{y_0}}{(x_n \vee 1)^y} \right) \\
 (13)
 \end{aligned}$$

$$+ \sum_{\substack{y \rightarrow y' \in \mathcal{R} \\ y' \succ_D y}} \frac{\kappa_{y \rightarrow y'} \lambda_y(x_n)}{\lambda_{y_0}(x_n)} \ln \left(\frac{(x_n \vee 1)^{y'}}{(x_n \vee 1)^{y_0}} \right).$$

By Lemma 6, a part of term (12) can be shown to be bounded:

$$\lim_{n \rightarrow \infty} \frac{\kappa_{y \rightarrow y'} \lambda_y(x_n)}{\lambda_{y_0}(x_n)} \frac{(x_n \vee 1)^{y_0}}{(x_n \vee 1)^y} = \begin{cases} \kappa_{y \rightarrow y'} & \text{if } y \notin T_{\{x_n\}}^{S, \infty}, \\ 0 & \text{if } y \in T_{\{x_n\}}^{S, \infty}. \end{cases}$$

In addition, since $y_0 \in T_{\{x_n\}}^{D, 1}$ and $y \notin T_{\{x_n\}}^{D, 1}$,

$$\lim_{n \rightarrow \infty} \frac{(x_n \vee 1)^y}{(x_n \vee 1)^{y_0}} \ln \left(\frac{(x_n \vee 1)^{y_0}}{(x_n \vee 1)^y} \right) = 0,$$

where we are utilizing $\lim_{t \rightarrow 0^+} t \ln(1/t) = 0$. We conclude that the term (12) converges to zero as $n \rightarrow \infty$. Finally, (11) shows that the term (13) is uniformly bounded in n .

We now turn to showing that term II converges to $-\infty$ as $n \rightarrow \infty$. We have

$$\begin{aligned}
 \text{II} &= \sum_{\substack{y \rightarrow y' \in \mathcal{R} \\ y \succ_D y'}} \frac{\kappa_{y \rightarrow y'} \lambda_y(x_n)}{\lambda_{y_0}(x_n)} \ln \left(\frac{(x_n \vee 1)^{y'}}{(x_n \vee 1)^y} \right) \\
 (14) \\
 &= \frac{\kappa_{y_0 \rightarrow y'_0} \lambda_{y_0}(x_n)}{\lambda_{y_0}(x_n)} \ln \left(\frac{(x_n \vee 1)^{y'_0}}{(x_n \vee 1)^{y_0}} \right) + \sum_{\substack{y \rightarrow y' \in \mathcal{R} \setminus \{y_0 \rightarrow y'_0\} \\ y \succ_D y'}} \frac{\kappa_{y \rightarrow y'} \lambda_y(x_n)}{\lambda_{y_0}(x_n)} \ln \left(\frac{(x_n \vee 1)^{y'}}{(x_n \vee 1)^y} \right),
 \end{aligned}$$

where we recall that y'_0 is the product complex of the descending reaction $y_0 \rightarrow y'_0$. Note that the first term on the right of (14) converges to $-\infty$ since $\kappa_{y_0 \rightarrow y'_0} > 0$ and

$$\lim_{n \rightarrow \infty} \ln \left(\frac{(x_n \vee 1)^{y'_0}}{(x_n \vee 1)^{y_0}} \right) = -\infty.$$

The second term on the right of (14) may be an empty sum. However, if there are any terms in the sum, they must be less than or equal to zero for n large enough. Indeed, this follows because

$$\lim_{n \rightarrow \infty} \ln \left(\frac{(x_n \vee 1)^{y'}}{(x_n \vee 1)^y} \right) = -\infty$$

and $\lambda_y(x_n) \geq 0$. Therefore, we conclude that the term II converges to $-\infty$ as $n \rightarrow \infty$.

Hence, we must conclude that $\lim_{n \rightarrow \infty} \mathcal{A}V(x_n) = -\infty$. However, this is in contradiction to the assumption that we made at the beginning of this proof, and the result is shown. \square

We have following corollary of Theorem 9.

COROLLARY 10. *Let $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ be a reaction network. Suppose that*

$$D_{\{x_n\}} \neq \emptyset \quad \text{and} \quad T_{\{x_n\}}^{D,1} = T_{\{x_n\}}^{S,1}$$

for any tier-sequence $\{x_n\}$. Then for any choice of rate constants the Markov process with intensity functions (4) associated to the reaction network $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ satisfies the following: each state in a closed, irreducible component of the state space is positive recurrent; moreover, if τ_{x_0} is the time for the process to enter the union of the closed irreducible components given an initial condition x_0 , then $\mathbb{E}[\tau_{x_0}] < \infty$.

5. Network structures that guarantee positive recurrence. With Theorem 9 and Corollary 10 in hand, we turn to proving our main results: Theorems 1 and 2.

5.1. The single linkage class case. In the papers [3, 4] it was shown that deterministic models of reaction networks with a single weakly reversible linkage class were persistent and bounded. In this section, we generalize this result to the stochastic setting with the additional assumption that all in-flows and out-flows are present. We begin with a lemma.

LEMMA 11. *Let $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ be a reaction network with $\mathcal{S} = \{S_1, S_2, \dots, S_d\}$. Suppose $S_i \rightarrow \emptyset \in \mathcal{R}$ for some species S_i . For a tier-sequence $\{x_n\}$, if $S_i \in T_{\{x_n\}}^{D,1}$, then*

$$(15) \quad S_i \in T_{\{x_n\}}^{S,1} \cap D_{\{x_n\}}.$$

Proof. Note that Lemma 5 implies $\emptyset \notin T_{\{x_n\}}^{D,1}$. Hence, $S_i \in D_{\{x_n\}}$. Because $\lambda_{S_i}(x_n) \neq 0$, Corollary 7 implies $S_i \in T_{\{x_n\}}^{S,1}$. \square

We now prove Theorem 1, which we restate here.

THEOREM 1. *Let $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ be a weakly reversible, binary reaction network that has a single linkage class. Let $\tilde{\mathcal{R}} = \mathcal{R} \cup_{S \in \mathcal{S}} \{\emptyset \rightarrow S, S \rightarrow \emptyset\}$ and $\tilde{\mathcal{C}} = \mathcal{C} \cup \{\emptyset\} \cup \{S \mid S \in \mathcal{S}\}$. Then, for any choice of rate constants, every state of the Markov process with intensity functions (4) associated to the reaction network $(\mathcal{S}, \tilde{\mathcal{C}}, \tilde{\mathcal{R}})$ is positive recurrent.*

Proof. For concreteness, order the species as $\mathcal{S} = \{S_1, \dots, S_d\}$.

First suppose \mathcal{C} consists of either only binary complexes or only unary complexes. Then $(y' - y) \cdot \vec{1} = 0$ for all $y \rightarrow y' \in \mathcal{R}$, where $\vec{1} = (1, 1, \dots, 1) \in \mathbb{Z}^d$. Let \mathcal{A} be a generator of the Markov process associated to the reaction network $(\mathcal{S}, \tilde{\mathcal{C}}, \tilde{\mathcal{R}})$. Then for the function $W(x) = x_1 + x_2 + \dots + x_d$, we have

$$\mathcal{A}W(x) = - \sum_{i=1}^d \kappa_{S_i \rightarrow \emptyset} x_i + \sum_{i=1}^d \kappa_{\emptyset \rightarrow S_i}.$$

Thus, for an arbitrary sequence $\{x_n\} \in \mathbb{Z}_{\geq 0}^d$ such that $|x_n| \rightarrow \infty$ as $n \rightarrow \infty$,

$$\mathcal{A}W(x_n) \rightarrow -\infty.$$

This implies $\mathcal{A}W(x) < -1$ for all x but finitely many. Hence, we may apply Theorem 3. Noting that weak reversibility implies that all states are contained within a closed, irreducible component of the state space then finishes the proof.

Now we suppose \mathcal{C} does not contain only binary complexes or only unary complexes. Let $\{x_n\}$ be a tier-sequence. We will show that (9) holds for the expanded network $(\mathcal{S}, \tilde{\mathcal{C}}, \tilde{\mathcal{R}})$, in which case an application of Theorem 9 is applicable. Noting that weak reversibility implies that all states are contained within a closed, irreducible component of the state space then finishes the proof.

There are three cases to consider.

Case 1. Assume that all complexes in \mathcal{C} are in $T_{\{x_n\}}^{D,1}$.

If there is no unary complex in \mathcal{C} , then we must have $\emptyset \in \mathcal{C}$ (since not all complexes are binary). However, by Lemma 5 we know $\emptyset \notin T_{\{x_n\}}^{D,1}$. Since this would contradict that all complexes in \mathcal{C} are in $T_{\{x_n\}}^{D,1}$, it must be that at least one unary complex is in \mathcal{C} . Since a unary complex is in $T_{\{x_n\}}^{D,1}$, Lemma 11 implies $D_{\{x_n\}} \cap T_{\{x_n\}}^{S,1} \neq \emptyset$.

Case 2. Assume that some of the complexes in \mathcal{C} are not in $T_{\{x_n\}}^{D,1}$, and one complex in $D_{\{x_n\}}$ is binary.

Since (i) not all complexes in \mathcal{C} are in $T_{\{x_n\}}^{D,1}$, and (ii) $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ is weakly reversible, there is a reaction $y_0 \rightarrow y'_0$ such that $y_0 \in T_{\{x_n\}}^{D,1}$ and $y'_0 \notin T_{\{x_n\}}^{D,1}$. We assume that $y_0 = S_i + S_j$ for some $i, j \in \{1, 2, \dots, d\}$ (where we allow $i = j$).

If $y_0 \in T_{\{x_n\}}^{S,1}$, then we may conclude the proof by an application of Theorem 9. Hence, we assume that $y_0 \notin T_{\{x_n\}}^{S,1}$, and we must demonstrate the existence of a descending reaction $y \rightarrow y'$ such that $y \in T_{\{x_n\}}^{S,1}$.

By Corollary 7, we must have $y_0 \in T_{\{x_n\}}^{S,\infty}$. This means $i \neq j$ and, without loss of generality, $x_{n,j} = 0$ for all n . We further conclude from Lemma 5 that $x_{n,i} \rightarrow \infty$ as $n \rightarrow \infty$. Also, since $S_i + S_j \in T_{\{x_n\}}^{D,1}$, it must be that $S_i \in T_{\{x_n\}}^{D,1}$ since when $x_{n,j} = 0$, we have

$$(x_n \vee 1)^{S_i} = x_{n,i} = x_{n,i} \cdot (x_{n,j} \vee 1) = (x_n \vee 1)^{S_i + S_j}.$$

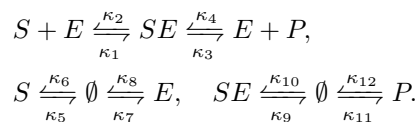
An application of Lemma 11 then completes the argument.

Case 3. Assume that some of the complexes in \mathcal{C} are not in $T_{\{x_n\}}^{D,1}$, and one complex in $D_{\{x_n\}}$ is unary.

An application of Lemma 11 completes the argument. □

Consider the following example of substrate-enzyme kinetics.

Example 4.



This reaction network consists of a single linkage class which is weakly reversible (the top linkage class) and in-flows and out-flows for all species. Moreover, the state space $\mathbb{S} = \mathbb{Z}_{\geq 0}^4$ is irreducible. Therefore the associated Markov process for this reaction network is positive recurrent for any choice of rate constants $\kappa_1, \kappa_2, \dots, \kappa_{12}$.

5.2. Double-full binary reaction networks. In this section, we prove Theorem 2. We begin with a necessary lemma that captures the usefulness of the double-full assumption.

LEMMA 12. Let $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ be a double-full, binary reaction network with $\mathcal{S} = \{S_1, S_2, \dots, S_d\}$. Let $\{x_n\}$ be a tier-sequence of $(\mathcal{S}, \mathcal{C}, \mathcal{R})$. Then the following holds:

1. If $S_i + S_j \in T_{\{x_n\}}^{D,1}$, then $2S_i, 2S_j \in T_{\{x_n\}}^{D,1}$. Thus, $\lim_{n \rightarrow \infty} \frac{(x_{n,i} \vee 1)}{(x_{n,j} \vee 1)} = C$ for some constant $C > 0$.
2. $T_{\{x_n\}}^{D,1} \subset \{S_i + S_j \mid i, j = 1, 2, \dots, d\}$ and $2S_i \in T_{\{x_n\}}^{D,1}$ for some $i = 1, 2, \dots, d$. That is, $T_{\{x_n\}}^{D,1}$ consists of only binary complexes and always contains at least one double complex.
3. $T_{\{x_n\}}^{D,1} = T_{\{x_n\}}^{S,1}$.

Proof. Let $I = \{i \mid \lim_{n \rightarrow \infty} x_{n,i} = \infty\}$.

For the first claim, if $i = j$, then the result is trivial. Thus, let $i \neq j$. Suppose $2S_i \notin T_{\{x_n\}}^{D,1}$. Then

$$\lim_{n \rightarrow \infty} \frac{(x_n \vee 1)^{2S_i}}{(x_n \vee 1)^{S_i + S_j}} = \lim_{n \rightarrow \infty} \frac{(x_{n,i} \vee 1)}{(x_{n,j} \vee 1)} = 0.$$

Hence,

$$\lim_{n \rightarrow \infty} \frac{(x_n \vee 1)^{S_i + S_j}}{(x_n \vee 1)^{2S_j}} = \lim_{n \rightarrow \infty} \frac{(x_{n,i} \vee 1)}{(x_{n,j} \vee 1)} = 0.$$

This implies $2S_j \succ_D S_i + S_j$ which is in contradiction to the assumption $S_i + S_j \in T_{\{x_n\}}^{D,1}$. Therefore, $2S_i \in T_{\{x_n\}}^{D,1}$. In same way, we can show $2S_j \in T_{\{x_n\}}^{D,1}$.

We turn to the second claim. We will show that unary complexes and the zero complex cannot be in $T_{\{x_n\}}^{D,1}$. First $\emptyset \notin T_{\{x_n\}}^{D,1}$ follows by Lemma 5. Suppose now that $S_m \in T_{\{x_n\}}^{D,1}$ for some m . Then either $2S_m \succ_D S_m$ or $2S_k \succ_D S_m$ for some $k \in I$, because

$$\begin{aligned} \lim_{n \rightarrow \infty} \frac{(x_n \vee 1)^{S_m}}{(x_n \vee 1)^{2S_m}} &= \lim_{n \rightarrow \infty} \frac{1}{x_{n,m}} = 0 \quad \text{if } m \in I \quad \text{and} \\ \lim_{n \rightarrow \infty} \frac{(x_n \vee 1)^{S_m}}{(x_n \vee 1)^{2S_k}} &= \lim_{n \rightarrow \infty} \frac{x_{n,m}}{x_{n,k}^2} = 0 \quad \text{if } m \notin I. \end{aligned}$$

Thus $S_m \notin T_{\{x_n\}}^{D,1}$. Result 1 of Lemma 12 shows that there is at least one i for which $2S_i \in T_{\{x_n\}}^{D,1}$.

For the last claim, we will first show that $T_{\{x_n\}}^{S,1} \subset T_{\{x_n\}}^{D,1}$. Let $y \in T_{\{x_n\}}^{S,1}$. By result 2 in Lemma 12, $2S_i \in T_{\{x_n\}}^{D,1}$ for some i . Note that, by Corollary 7, $2S_i \in T_{\{x_n\}}^{S,1}$ since Lemma 5 implies that $\lambda_{2S_i}(x_n) \neq 0$ for large n . Applying Lemma 6, we have

$$\lim_{n \rightarrow \infty} \frac{(x_n \vee 1)^{2S_i}}{(x_n \vee 1)^y} = \lim_{n \rightarrow \infty} \frac{\lambda_{2S_i}(x_n)}{\lambda_y(x_n)} = C \quad \text{for some constant } C > 0.$$

This means that $y \sim_D 2S_i$. Therefore $y \in T_{\{x_n\}}^{D,1}$, and we conclude that $T_{\{x_n\}}^{S,1} \subset T_{\{x_n\}}^{D,1}$. Now we will show $T_{\{x_n\}}^{D,1} \subset T_{\{x_n\}}^{S,1}$. Let $y \in T_{\{x_n\}}^{D,1}$. It is sufficient to show that $y \notin T_{\{x_n\}}^{S,\infty}$ by Corollary 7. By result 2, $y = S_i + S_j$ for some i and j (where we allow $i \neq j$), and $2S_i \in T_{\{x_n\}}^{D,1}$ and $2S_j \in T_{\{x_n\}}^{D,1}$. By Lemma 5, $x_{n,i} \rightarrow \infty$ and $x_{n,j} \rightarrow \infty$ as $n \rightarrow \infty$. Therefore $\lambda_y(x_n) \neq 0$ for large n , and hence $y \notin T_{\{x_n\}}^{S,\infty}$. \square

Lemma 12 concludes that $T_{\{x_n\}}^{D,1}$ and $T_{\{x_n\}}^{S,1}$ for a double-full, binary reaction network are always equal and consist of binary complexes. Now we restate the second main result Theorem 2 with its proof.

THEOREM 2. *Let $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ be a binary reaction network satisfying the following two conditions:*

1. *the reaction network is double-full, and*
2. *for each double complex (of the form $2S_i$) there is a directed path within the reaction graph beginning with the double complex itself and ending with either a unary complex (of the form S_j) or the zero complex.*

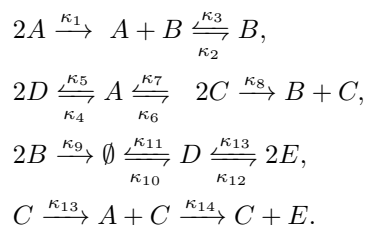
Then, for any choice of rate constants, the Markov process with intensity functions (4) associated to the reaction network $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ satisfies the following: each state in a closed, irreducible component of the state space is positive recurrent; moreover, if τ_{x_0} is the time for the process to enter the union of the closed irreducible components given an initial condition x_0 , then $\mathbb{E}[\tau_{x_0}] < \infty$.

Proof. Let $\{x_n\}$ be a tier-sequence. Result 3 in Lemma 12 shows $T_{\{x_n\}}^{D,1} = T_{\{x_n\}}^{S,1}$. Thus, so long as a descending reaction can be shown to exist, an application of Corollary 10 will complete the proof.

By result 2 in Lemma 12, there exists a double complex $2S_i \in T_{\{x_n\}}^{D,1}$ for some i . By our hypothesis, there exists a directed path from $2S_i$ to a unary or the zero complex y' in the reaction graph. According to result 2 in Lemma 12, $y' \notin T_{\{x_n\}}^{D,1}$. Therefore a descending reaction exists within the directed path from $2S_i$ to y' . \square

We demonstrate Theorem 2 with an example.

Example 5. The following reaction network contains 5 species, 14 complexes and 14 reactions.



This binary reaction network is double-full. Moreover, for each double complex ($2A$, $2B$, $2C$, $2D$, $2E$, and $2F$), there is a directed path within the reaction graph beginning with the double complex itself and ending with either a unary complex or the zero complex. Therefore the conditions in Theorem 2 hold. Since $\mathbb{S} = \mathbb{Z}_{\geq 0}^5$ is irreducible for this model, the associated continuous-time Markov chain is positive recurrent regardless of choice of the rate constants $\kappa_1, \dots, \kappa_{14}$.

5.3. More results on double-full, binary reaction networks. In this section, we provide classes of double-full, binary reaction networks for which condition 2 of Theorem 2 (the “path condition”) does not hold but for which the conclusions of Theorem 2 still hold.

We begin with a technical lemma.

LEMMA 13. *Let $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ be a double-full, binary reaction network. Suppose the following:*

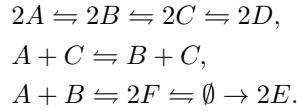
1. \mathcal{L} is a weakly reversible linkage class with $S, \tilde{S} \in \mathcal{S}(\mathcal{L})$ (where we allow $S = \tilde{S}$) such that $S + \tilde{S} \in \mathcal{C}$.

2. There is a directed path within the reaction graph beginning with $S + \tilde{S}$ and ending with a unary or the zero complex.

Then for any tier-sequence $\{x_n\}$ the following holds: if there is a complex y in the linkage class \mathcal{L} (i.e. $y \in \mathcal{C}(\mathcal{L})$) that is in $T_{\{x_n\}}^{D,1}$, then $D_{\{x_n\}} \neq \emptyset$.

We demonstrate the lemma with an example.

Example 6. Consider the following reaction network:



Let \mathcal{L} be the middle linkage class (i.e., $A + C \rightleftharpoons B + C$). Then, $A, B \in \mathcal{S}(\mathcal{L})$, and there is a directed path from $A + B$ to \emptyset , showing that conditions 1 and 2 of Lemma 13 are met. Hence, we conclude that if $\{x_n\}$ is a tier-sequence and either $A + C$ or $B + C$ are in $T_{\{x_n\}}^{D,1}$, then we necessarily have that $D_{\{x_n\}} \neq \emptyset$. In this case, the descending reaction could be in any of the three linkage classes (depending upon the particular sequence $\{x_n\}$).

Proof. Let $\mathcal{S} = \{S_1, S_2, \dots, S_d\}$. Assume that $\{x_n\}$ is a tier-sequence and that there is a $y \in \mathcal{C}(\mathcal{L})$ such that $y \in T_{\{x_n\}}^{D,1}$. We must show that $D_{\{x_n\}} \neq \emptyset$.

Case 1. If there is a complex $y' \in \mathcal{C}(\mathcal{L})$ that is not in $T_{\{x_n\}}^{D,1}$, then there necessarily exists a descending reaction along $\{x_n\}$ by the weak reversibility of \mathcal{L} .

Case 2. Now suppose that all complexes in $\mathcal{C}(\mathcal{L})$ are in $T_{\{x_n\}}^{D,1}$. We will show $S + \tilde{S} \in T_{\{x_n\}}^{D,1}$. We assume $S = S_i$ and $\tilde{S} = S_j$ for some i and j (where, again, we could have $i = j$). By result 2 in Lemma 12, $\mathcal{C}(\mathcal{L})$ contains only binary complexes. Thus $S_i + S_m \in \mathcal{C}(\mathcal{L})$ for some m . Indices i, j , and m are not necessarily all distinct. By result 1 in Lemma 12, $\{2S_i, 2S_m, 2S_j\} \subset T_{\{x_n\}}^{D,1}$. Therefore

$$\lim_{n \rightarrow \infty} \frac{(x_n \vee 1)^{S_i + S_j}}{(x_n \vee 1)^{S_i + S_m}} = \lim_{n \rightarrow \infty} \frac{(x_{n,j} \vee 1)}{(x_{n,m} \vee 1)} = \sqrt{\lim_{n \rightarrow \infty} \frac{(x_n \vee 1)^{2S_j}}{(x_n \vee 1)^{2S_m}}} = C \quad \text{for some } C > 0.$$

Therefore $S_i + S_j \in T_{\{x_n\}}^{D,1}$. By hypothesis 2 of Lemma 13, there exists a directed path from $S_i + S_j$ to a unary complex or the zero complex within the reaction graph. Since only binary complexes can be in $T_{\{x_n\}}^{D,1}$ in a double-full reaction network, there exists a descending reaction along $\{x_n\}$ within the directed path. \square

THEOREM 14. Let $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ be a double-full, binary reaction network with linkage classes $\mathcal{L}_1, \mathcal{L}_2, \dots, \mathcal{L}_\ell$. Suppose there is an integer $m \in \{1, 2, \dots, \ell - 1\}$ such that the following hold:

1. For $i \leq m$, \mathcal{L}_i is weakly reversible and $\mathcal{C}(\mathcal{L}_i)$ contains only binary complexes.
2. For each $i \leq m$, there exists $S, \tilde{S} \in \mathcal{S}(\mathcal{L}_i)$ (where we allow $S \neq \tilde{S}$) such that
 - (i) $S + \tilde{S} \in \mathcal{C}$,
 - (ii) there is a directed path within the reaction graph beginning with $S + \tilde{S}$ and ending with a unary or the zero complex.
3. For each double complex $2S$, either $2S \in \mathcal{C}(\mathcal{L}_i)$ for some $i \leq m$ or there is a directed path within the reaction graph beginning with $2S$ and ending with a unary complex or the zero complex.

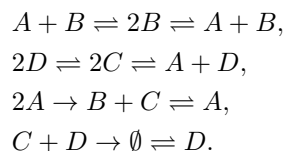
Then, for any choice of rate constants, the Markov process with intensity functions (4) associated to the reaction network $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ satisfies the following: each state in a closed, irreducible component of the state space is positive recurrent; moreover, if τ_{x_0} is the time for the process to enter the union of the closed irreducible components given an initial condition x_0 , then $\mathbb{E}[\tau_{x_0}] < \infty$.

Proof. Let $\{x_n\}$ be a tier-sequence. Result 3 in Lemma 12 shows $T_{\{x_n\}}^{D,1} = T_{\{x_n\}}^{S,1}$. Thus, so long as a descending reaction can be shown to exist, an application of Corollary 10 will complete the proof.

By result 2 in Lemma 12, $2S_j \in T_{\{x_n\}}^{D,1}$ for some j . If there is a directed path beginning with $2S_j$ and ending with a unary complex or the zero complex within the reaction graph, we have a descending reaction along $\{x_n\}$ within the directed path. Otherwise, $2S_j \in \mathcal{C}(\mathcal{L}_i)$ for some $i \leq m$ by the hypothesis, and hence $D_{\{x_n\}} \neq \emptyset$ by Lemma 13. \square

We demonstrate Theorem 14 with an example.

Example 7. Consider the following, which is a double-full, binary reaction network for which the conditions in Theorem 14 hold.



Note that Theorem 2 stands silent on this model as there is no reaction path beginning with $2B$ and ending with a unary complex or \emptyset .

Let $\mathcal{L}_1, \mathcal{L}_2, \mathcal{L}_3$, and \mathcal{L}_4 be the linkage classes of this reaction network in order from top to bottom. We demonstrate that the assumptions of Theorem 14 are fulfilled with $m = 2$.

1. The linkage classes \mathcal{L}_1 and \mathcal{L}_2 contain only binary complexes and are weakly reversible.
2. (i) For linkage class \mathcal{L}_1 , we take $S = \tilde{S} = A$ and note the path from $2A$ to A in \mathcal{L}_3 .
(ii) For linkage class \mathcal{L}_2 , we take $S = C$ and $\tilde{S} = D$ and note the reaction $C + D \rightarrow \emptyset$ in \mathcal{L}_4 .
3. We note $2B \in \mathcal{L}_1$ and $2C, 2D \in \mathcal{L}_2$. Also, there is a path from $2A$ to A in \mathcal{L}_3 .

Since weak reversibility guarantees the existence of a directed path between two complexes within any linkage class, we can modify the conditions in Theorem 14.

COROLLARY 15. *Let $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ be a weakly reversible, double-full, binary reaction network with linkage classes $\mathcal{L}_1, \mathcal{L}_2, \dots, \mathcal{L}_\ell$. Let $m \in \{1, \dots, \ell - 1\}$, and suppose the following:*

1. $\mathcal{C}(\mathcal{L}_i)$ contains only binary complexes for each $i \leq m$, and $\mathcal{C}(\mathcal{L}_i)$ contains at least one non-binary complex for each $i > m$.
2. For each $i \leq m$, there exist species $S, \tilde{S} \in \mathcal{C}(\mathcal{L}_i)$ such that $S + \tilde{S} \in \mathcal{C}(\mathcal{L}_j)$ for some $j > m$.

Then, for any choice of rate constants, every state of the Markov process with intensity functions (4) associated to the reaction network $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ is positive recurrent.

Now we will provide another class of double-full, binary reaction networks in which we will assume the existence of out-flows.

THEOREM 16. Let $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ be a double-full, binary reaction network with linkage classes $\mathcal{L}_1, \mathcal{L}_2, \dots, \mathcal{L}_\ell$. Suppose there is an $m \in \{1, \dots, \ell - 1\}$ such that the following three conditions hold:

1. For each $i \leq m$, \mathcal{L}_i is weakly reversible and $\mathcal{C}(\mathcal{L}_i)$ contains only binary complexes.
2. For each $i > m$, $\mathcal{C}(\mathcal{L}_i)$ contains no binary complex.
3. For each $i \leq m$, there exists an $S \in \mathcal{S}(\mathcal{L}_i)$ such that $S \rightarrow \emptyset \in \mathcal{R}$.

Then, for any choice of rate constants, the Markov process with intensity functions (4) associated to the reaction network $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ satisfies the following: each state in a closed, irreducible component of the state space is positive recurrent; moreover, if τ_{x_0} is the time for the process to enter the union of the closed irreducible components given an initial condition x_0 , then $\mathbb{E}[\tau_{x_0}] < \infty$.

Proof. Let $\mathcal{S} = \{S_1, S_2, \dots, S_d\}$, and for some $0 < \delta < 1$ let

$$T(x) = (x_1 + x_2 + \dots + x_d)^{2+\delta} = (\vec{1} \cdot x)^{2+\delta},$$

where $\vec{1} = (1, 1, \dots, 1)^T \in \mathbb{Z}_{\geq 0}^d$. Let $\{x_n\}$ be a tier-sequence of $(\mathcal{S}, \mathcal{C}, \mathcal{R})$. We will show that

$$\lim_{n \rightarrow \infty} \mathcal{A}(V + T)(x_n) = -\infty.$$

An application of Theorem 3 then completes the proof.

We begin by finding relevant upper bounds for $\mathcal{A}T(x_n)$ in a similar fashion as Lemma 8. First, we define

$$I = \{i \mid \lim_{n \rightarrow \infty} x_{n,i} = \infty\}, \quad U = \{i \mid S_i \rightarrow \emptyset \in \mathcal{R}\}, \quad \text{and} \quad V = \{i \mid \emptyset \rightarrow S_i \in \mathcal{R}\}.$$

Since $(1 + h)^{2+\delta} = 1 + (2 + \delta)h + o(h) \leq 1 + 3h$ for h small enough, there is a positive constant K such that, for large n ,

$$\begin{aligned} \mathcal{A}T(x_n) &= \sum_{y \rightarrow y' \in \mathcal{R}} \lambda_{y \rightarrow y'}(x_n) ((\vec{1} \cdot x_n + \vec{1} \cdot (y' - y))^{2+\delta} - (\vec{1} \cdot x_n)^{2+\delta}) \\ &= (\vec{1} \cdot x_n)^{2+\delta} \sum_{y \rightarrow y' \in \mathcal{R}} \lambda_{y \rightarrow y'}(x_n) \left(\left(1 + \frac{\vec{1} \cdot (y' - y)}{\vec{1} \cdot x_n} \right)^{2+\delta} - 1 \right) \\ &\leq 3(\vec{1} \cdot x_n)^{2+\delta} \sum_{y \rightarrow y' \in \mathcal{R}} \lambda_{y \rightarrow y'}(x_n) \left(\frac{\vec{1} \cdot (y' - y)}{\vec{1} \cdot x_n} \right) \\ &= 3(\vec{1} \cdot x_n)^{1+\delta} \sum_{y \rightarrow y' \in \mathcal{R}} \lambda_{y \rightarrow y'}(x_n) (\vec{1} \cdot (y' - y)) \\ &= 3(\vec{1} \cdot x_n)^{1+\delta} \left(\sum_{i \in U} \lambda_{S_i \rightarrow \emptyset}(x_n) (-1) + \sum_{i \in V} \lambda_{\emptyset \rightarrow S_i}(x_n) \right) \\ (16) \quad &\leq 3(\vec{1} \cdot x_n)^{1+\delta} \left(- \sum_{i \in U \cap I} \kappa_{S_i \rightarrow \emptyset} x_{n,i} + K \right). \end{aligned}$$

Therefore, if there is $k \in U \cap I$ such that

$$\lim_{n \rightarrow \infty} \frac{(x_{n,k} \vee 1)}{(x_{n,i} \vee 1)} \quad \text{exists and} \quad \lim_{n \rightarrow \infty} \frac{(x_{n,k} \vee 1)}{(x_{n,i} \vee 1)} > 0$$

for all $i \in \{1, 2, 3, \dots, d\}$, then there is a constant $K' > 0$ such that

$$(17) \quad \mathcal{A}T(x_n) \leq -K' x_{n,k}^{2+\delta}$$

for large n . Hence, we have found our bound on $\mathcal{A}T$, and we turn to $\mathcal{A}(T + V)$.

Note that by result 2 in Lemma 12 there is an i for which $2S_i \in T_{\{x_n\}}^{D,1}$. Without loss of generality, we assume $i = 1$ and $2S_1 \in \mathcal{C}(\mathcal{L}_1)$. There are two cases to consider: (i) $\mathcal{C}(\mathcal{L}_1) \subseteq T_{\{x_n\}}^{D,1}$ and (ii) there is a complex $y' \in \mathcal{C}(\mathcal{L}_1)$ such that $y' \notin T_{\{x_n\}}^{D,1}$.

Case 1. Suppose $\mathcal{C}(\mathcal{L}_1) \subseteq T_{\{x_n\}}^{D,1}$. Then by hypothesis 3 of Theorem 16, there exists a species, say, S_k , such that $S_k \in \mathcal{S}(\mathcal{L}_1)$ and $S_k \rightarrow \emptyset \in \mathcal{R}$. Note that $S_k + S_j \in \mathcal{C}(\mathcal{L}_1) \subseteq T_{\{x_n\}}^{D,1}$ for some j (where we allow $k = j$) because $\mathcal{C}(\mathcal{L}_1)$ only contains binary complexes. By result 1 in Lemma 12, $2S_k \in T_{\{x_n\}}^{D,1}$ and hence $k \in U \cap I$ by Lemma 5. Since $2S_k \in T_{\{x_n\}}^{D,1}$ and the network is double-full, for all $i = 1, 2, 3, \dots, d$ we have

$$\lim_{n \rightarrow \infty} \frac{(x_{n,k} \vee 1)}{(x_{n,i} \vee 1)} \text{ exists and } \lim_{n \rightarrow \infty} \frac{(x_{n,k} \vee 1)}{(x_{n,i} \vee 1)} > 0.$$

Hence, by (17) there is a constant $K' > 0$ such that for large n ,

$$(18) \quad \mathcal{A}T(x_n) \leq -K' x_{n,k}^{2+\delta}.$$

We now turn to $\mathcal{A}V$. Note that $T_{\{x_n\}}^{D,1} = T_{\{x_n\}}^{S,1}$ by result 3 in Lemma 12. Since $2S_k \in T_{\{x_n\}}^{D,1} = T_{\{x_n\}}^{S,1}$ there is a constant $K'' > 0$ such that

$$(19) \quad \lim_{n \rightarrow \infty} \frac{\lambda_y(x_n)}{\lambda_{2S_k}(x)} \leq K'' \quad \text{and} \quad \lim_{n \rightarrow \infty} \frac{(x_n \vee 1)^y}{(x_n \vee 1)^{2S_k}} \leq K''$$

for any complex $y \in \mathcal{C}$. Now applying Lemma 8 and (19), we may conclude that there are positive constants C and C' such that

$$\mathcal{A}V(x_n) \leq \sum_{y \rightarrow y' \in \mathcal{R}} \kappa_{y \rightarrow y'} \lambda_y(x_n) \left(\ln \frac{(x_n \vee 1)^{y'}}{(x_n \vee 1)^y} + C \right) \leq C' \lambda_{2S_k}(x_n) \ln(x_{n,k}^2)$$

for large n . Hence, combining our estimates for $\mathcal{A}T$ and $\mathcal{A}V$,

$$\mathcal{A}(V + T)(x_n) \leq C' \lambda_{2S_k}(x_n) \ln(x_{n,k}^2) - K' x_{n,k}^{2+\delta} \rightarrow -\infty \quad \text{as } n \rightarrow \infty.$$

Case 2. We now suppose that there is a complex $y' \in \mathcal{C}(\mathcal{L}_1)$ such that $y' \notin T_{\{x_n\}}^{D,1}$. Since \mathcal{L}_1 is weakly reversible, there exists a directed path beginning with $2S_1$ and ending with y' . Thus there is a descending reaction $y_0 \rightarrow y'_0$ along $\{x_n\}$ within the directed path. Note that $y_0 \in T_{\{x_n\}}^{S,1}$ because $T_{\{x_n\}}^{D,1} = T_{\{x_n\}}^{S,1}$ by result 3 in Lemma 12 and, hence, $y_0 \in T_{\{x_n\}}^{S,1} \cap D_{\{x_n\}}$. Since terms I, III, IV in (10) are uniformly bounded in n and term II converges to $-\infty$, as $n \rightarrow \infty$,

$$(20) \quad \mathcal{A}V(x_n) \leq -\lambda_{y_0}(x_n) \quad \text{for large } n.$$

By Lemma 6 and the fact that $y_0 \in T_{\{x_n\}}^{D,1} = T_{\{x_n\}}^{S,1}$, there is a constant $C \geq 0$ such that for any $k \in I$,

$$\lim_{n \rightarrow \infty} \frac{x_{n,k}}{\sqrt{\lambda_{y_0}(x_n)}} = \lim_{n \rightarrow \infty} \sqrt{\frac{(x_{n,k} \vee 1)^{2S_k}}{\lambda_{y_0}(x_n)}} = \lim_{n \rightarrow \infty} \sqrt{\frac{(x_{n,k} \vee 1)^{2S_k}}{(x_n \vee 1)^{y_0}}} \sqrt{\frac{(x_n \vee 1)^{y_0}}{\lambda_{y_0}(x_n)}} = C.$$

Therefore, there is a constant $C' > 0$ such that

$$(21) \quad (\vec{1} \cdot x_n)^{1+\delta} = (x_{n,1} + x_{n,2} + \dots + x_{n,d})^{1+\delta} \leq C'' \lambda_{y_0}(x_n)^{(1+\delta)/2}.$$

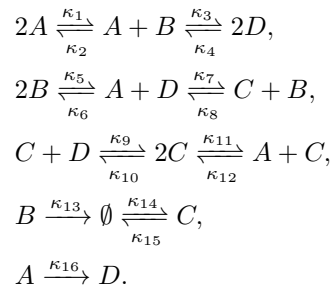
Note that $\lambda_{y_0}(x_0) \rightarrow \infty$, as $n \rightarrow \infty$ by Corollary 7. Then by (16), (20), and (21), there are constants $C''' > 0$ such that

$$\mathcal{A}(V + T)(x_n) \leq -\lambda_{y_0}(x_n) + C''' \lambda_{y_0}(x_n)^{(1+\delta)/2} \rightarrow \infty \quad \text{as } n \rightarrow \infty,$$

because $\delta < 1$. □

We demonstrate Theorem 16 with an example.

Example 8. Consider the following double-full, binary reaction network with 16 reactions.



Let $\mathcal{L}_1, \dots, \mathcal{L}_5$ be the linkage classes of this reaction network in order from top to bottom. We verify the conditions of Theorem 16 with $m = 3$.

1. $\mathcal{L}_1, \mathcal{L}_2$, and \mathcal{L}_3 are weakly reversible and contain only binary complexes.
2. \mathcal{L}_4 and \mathcal{L}_5 do not contain binary complexes.
3. Note that species $B \in S(\mathcal{L}_1)$, $B \in S(\mathcal{L}_2)$, and $C \in S(\mathcal{L}_3)$ satisfy the third condition of the theorem.

Moreover, $\mathbb{S} = \mathbb{Z}_{\geq 0}^4$ is irreducible. Therefore the associated continuous-time Markov chain for this reaction network is positive recurrent for any choice of rate constants $\kappa_1, \kappa_2, \dots, \kappa_{16}$.

6. Discussion. We introduced two main network conditions, each of which guarantees that each state in a closed, irreducible component of the state space is positive recurrent and that, regardless of initial condition, all trajectories enter a closed, irreducible component in finite time. The analysis was based on the idea of *tiers* introduced in [3, 4]. There are a number of avenues for future work.

First, we believe that *all* systems whose reaction networks are weakly reversible are positive recurrent, and the present work grew out of an attempt to prove this. Specifically, we believe the following to be true.

CONJECTURE (positive recurrence conjecture). *Let $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ be a weakly reversible reaction network. Then, for any choice of rate constants, every state of the Markov process with intensity functions (4) associated to the reaction network $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ is positive recurrent.*

Attempting to prove this conjecture, which is closely related to the global attractor conjecture [15, 16] for deterministic models, remains an active pursuit.

Second, a natural follow-up question is, how fast do the processes considered here converge to their stationary distributions? Results related to this question will be presented in a forthcoming paper.

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