ROBUST STABILITY OF PERTURBED CONTINUOUS-TIME MARKOV CHAINS

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Abstract:

This paper studies the stability of perturbed continuous-time Markov chains (CT-MCs) by establishing stability criteria and robustness indicators. The robust stability criteria are derived from the spatial relationships between reachable sets and invariant subsets. Moreover, a robustness indicator is formulated to quantify the ability of each transition to resist perturbations affecting the stability, where lower values signify more critical transitions. Finally, a biological case study demonstrates the applicability of the theoretical result. This framework not only facilitates stability assessments for perturbed CT-MCs but also identifies critical transitions, the monitoring of which can enhance system resilience.

Keywords:

Continuous-time Markov chain; Invariant subset; Perturbation; Robustness; Stability

1. Introduction

Continuous-time Markov chains (CT-MCs) represent a fundamental class of stochastic processes characterized by state transitions occurring in continuous time while satisfying the Markov property [1]. The process is uniquely defined by its transition rate matrix (TRM), also known as the infinitesimal generator [2], where the off-diagonal elements represent state transition rates and the diagonal elements enforce conservation conditions. Unlike discrete-time systems, CT-MCs directly model the intrinsic timing of events through transition rates rather than stepwise probabilities [3]. A CT-MC achieves ergodicity when there exists a unique stationary distribution that remains invariant under the time evolution of the system [4]. The system reaches stability when its probability distribution converges to this stationary distribution, indicating that the inflow and outflow probabilities are equilibrated for every state [5]. This steady-state distribution has profound physical interpretations: in chemical kinetics, it corresponds to chemical equilibrium concentrations [1]; in queueing theory, it represents steady-state service rates [6]; in gene regulatory networks, it characterizes long-term gene expression patterns that are typically associated with healthy cellular states, while deviations may lead to disease progression [7–9].

Functional perturbations in CT-MCs typically manifest as modifications to transition rates (e.g., due to environmental changes or mutations), which can potentially disrupt equilibrium distributions. For example, in gene regulatory networks, perturbations may arise from protein binding rate modifications or enzymatic activity shifts, leading to redefined steady-state distributions [10]. Similar concepts have been studied for Boolean networks, where perturbations modify logical update rules [10]. These binary logical systems admit a discrete-time Markov decision process representation [11], with dynamics satisfying the Markov property. In [12], a series of robust stabilization conditions is derived for perturbed Boolean control networks, requiring either 1) spatial separation between perturbed and controlled blocks, 2) accelerated convergence, or 3) unreachability of perturbed states. Recent extensions consider edge removal and edge sign switch, with stability criteria derived from reachability matrices [13]. However, current frameworks for both CT-MCs and Boolean networks lack a quantitative metric for edge/transition robustness and a determination criterion for critical edges that govern the system stability.

To effectively design resilient systems, it is essential to characterize how transition perturbations affect the stability of CT-MCs. In this work, we formally define robust stability as the ability of CT-MCs to maintain their stationary distributions when subjected to transition perturbations, particularly focusing on the case where the outgoing transition is redirected. In this context, we develop a systematic framework for quantifying the robust stability of CT-MCs. This framework involves calculating the reachable set to the target state, establishing robust stability criteria based on the spatial relationship between invariant sets and reachable sets, and finally providing a robustness indicator for each transition. In particular, this framework develops an approach for identifying critical transitions, especially those serving as topological bridges between network components, where perturbations may lead to system destabilization. By monitoring these critical transitions, we can identify potential vulnerabilities and enhance system resilience.

The remainder of this paper is organized as follows: In Section 2, the robust stability problem of perturbed CT-MCs is formulated. Section 3 presents the criteria for robust stability in CT-MCs, and Section 4 develops the robustness indicator. An example to illustrate the robustness analysis process is presented in Section 5, followed by the conclusion in Section 6.

2 Preliminaries

CT-MCs are mathematical models that are used to describe systems that transition between a finite number of states over continuous time. They are characterized by the following key components:

1) State Dynamics: The state of the system at time t is represented by the continuous-time homogeneous Markov process $x(t)$ over the finite state space $\mathscr{D}_n := \{1,2,\ldots,n\}$, which evolves according to the transition probability matrix (TPM) $P(t)$. The matrix elements are defined as

$$[P(t)]_{i,j} := \Pr\{x(\tau+t) = i \mid x(\tau) = j\},\ i,j \in \mathscr{D}_n, \qquad (1)$$

with the initial condition $P(0) = I_n$, where $\tau \geq 0$ indicates a specific initial time, and I_n is the $n\times n$ identity matrix.

2) Homogeneous Property: CT-MCs exhibit homogeneity, meaning that the TPM remains unchanged over time:

$$P(t+\tau) = P(t)P(\tau),\ \forall\, t,\tau \geq 0.$$

In this equation, $P(t)$ represents the TPM at time t, and $P(\tau)$ denotes the TPM over a time interval τ. The equality indicates that the probabilities of transitioning between states depend solely on the length of the time interval, rather than the specific time at which the transition occurs. This homogeneity property facilitates the derivation of long-term behaviors, such as stationary distributions, which are essential for understanding the equilibrium states of the Markov process.

3) Transition Rate Matrix (TRM): The TRM, denoted as Q, is defined as the limit of the derivative of the TPM:

$$Q := \lim_{t\to 0^+} \dot{P}(t) \in \mathbb{P}^{n\times n}. \qquad (2)$$

It satisfies $[Q]_{i,i} \leq 0$ for all $i \in \mathscr{D}_n$, $[Q]_{i,j} \geq 0$ for all $i,j \in \mathscr{D}_n$ with $i \neq j$, and $\sum_{i\in\mathscr{D}_n}[Q]_{i,j} = 0$ for all $j \in \mathscr{D}_n$.

4) Dynamics of the Probability Distribution Vector (PDV): Let $\mathbf{p}(t) \in \mathbb{P}^n$ represent the PDV for the state $x(t)$:

$$[\mathbf{p}(t)]_i = \Pr\{x(t) = i\},\ \forall\, i \in \mathscr{D}_n,$$

The evolution of the PDV is governed by the ordinary differential equation:

$$\begin{cases} \dot{\mathbf{p}}(t) = Q\mathbf{p}(t), \\ \mathbf{p}(0) = \mathbf{p}_0, \end{cases} \qquad (3)$$

where $\mathbf{p}_0 \in \mathbb{P}^n$ is the initial PDV. The solution to this system can be expressed as

$$\mathbf{p}(t;p_0) = e^{Qt}\mathbf{p}_0,$$

linking the time evolution of the PDV directly to the TRM Q. Thus, we refer to "CT-MC $\{Q\}$" as the CT-MC with TRM Q.

5) Network Structure: The network structure of a CT-MC is represented by its transition rate graph (TRG), denoted by a directed graph $\mathscr{G} = (\mathscr{D}_n,\mathscr{E})$ with $\mathscr{E} = \{(i,j) \in \mathscr{D}_n \times \mathscr{D}_n \mid [Q]_{j,i} > 0\}$. Each arc in $\mathscr{G}$ provides insight into the information flow within the CT-MC, such as flow direction (i.e., each arc (i,j) indicates that the system can transition from state i to state j at a rate defined by $[Q]_{j,i}$) and connectivity (i.e., the presence or absence of arcs helps to understand the connectivity and accessibility of the states within the network).

6) Stability: The asymptotical stability of CT-MC $\{Q\}$ to state $\alpha \in \mathscr{D}_n$ refers to the CT-MC starting from any state is reachable to state α and will not be transferred to other states. Here, we present the definitions of equilibrium point and stability for CT-MC $\{Q\}$.

Definition 2.1 (See [3]). *State $\alpha \in \mathscr{D}_n$ is said to be an equilibrium point of CT-MC $\{Q\}$ if*

$$\Pr\{x(t;x_0) = \alpha \mid x_0 = \alpha\} = 1,\ \forall\, t \geq 0. \qquad (4)$$

Definition 2.2 (See [3]). *CT-MC $\{Q\}$ is said to be asymptotically stable to $\alpha \in \mathscr{D}_n$, or simply α-stable, if*

$$\lim_{t\to+\infty} \Pr\{x(t;x_0) = \alpha\} = 1,\ \forall\, x_0 \in \mathscr{D}_n. \qquad (5)$$

3. Robust Stability of CT-MCs

Transition perturbation in CT-MCs refers to the alterations in transition rates that can influence the dynamics and stability of the system. For instance, in communication networks, variations in traffic load or failures of network links can be modeled as transition perturbations, which affect the flows of information and the overall performance of the network. Based on the stability definition of CT-MC $\{Q\}$, we precisely define transition perturbation and robust stability as follows.

Definition 3.1. *CT-MC $\{Q\}$ is said to undergo a transition perturbation, if a transition $(i,j)\in\mathscr{E}$ is altered to a new transition $(i,j')\in\mathscr{D}_n\times\mathscr{D}_n$. This perturbation is denoted as $(i,j)\rightsquigarrow(i,j')$ and is defined as*

$$\Delta Q=\Delta Q(i,j')-\Delta Q(i,j),$$

with $\Delta Q(i,k):=[Q]_{j,i}(e_{k,n}e_{i,n}^\top-e_{i,n}e_{i,n}^\top)$, $k=j,j'$, where $e_{\cdot,n}$ is the standard basis vector. The resulting CT-MC is expressed as CT-MC $\{Q'\}$ with $Q'=Q+\Delta Q$.

Definition 3.2. *Given an α-stable CT-MC $\{Q\}$, it is said to be robustly stable under perturbation $(i,j)\rightsquigarrow(i,j')$ if the resulting CT-MC $\{Q'\}$ satisfies the stability condition (5).*

Regarding $\alpha\in\mathscr{D}_n$, we define the l-step reachable set to α iteratively as follows:

$$\mathrm{R}[l]:=\begin{cases}\left\{i\in\mathscr{D}_n\backslash\bigcup_{k=1}^{l-1}\mathrm{R}[k]\mid[Q]_{j,i}>0,j\in\mathrm{R}[l-1]\right\}, & l>0\\ \{\alpha\}, & l=0.\end{cases}$$

Notably, if there exists an integer $L>0$ such that

$$\bigcup_{k=1}^{L}\mathrm{R}[k]=\mathscr{D}_n, \tag{6}$$

then CT-MC $\{Q\}$ achieves asymptotical α-stability. Hereafter, we define $l(i)$ as the index of the reachable set to which state i belongs, and denote $L^\star$ as the minimal integer such that equality (6) holds.

Next, regarding each state $i\in\mathscr{D}_n$, we define the vector to collect states in its preceding reachable sets and its reachable sets by

$$\mathbf{r}(i):=\sum_{k\in\bigcup_{r=0}^{l(i)}\mathrm{R}[r]}e_{k,n}^\top-e_{i,n}^\top. \tag{7}$$

Furthermore, we define the reachability matrix by

$$\mathbb{R}(i,j):=\sum_{l=1}^{n-\|\mathbf{r}(i)\|_0}\Big(Q-\Delta Q(i,j)\Big)^l. \tag{8}$$

Notably, if $j\notin\mathrm{R}[l(i)-1]$, then there exists a directed path from i through a state $\tilde{j}\in\mathrm{R}[l(i)-1]$ to α. This ensures the robust α-stability of CT-MC $\{Q\}$. Thus, we will focus on the case where $j\in\mathrm{R}[l(i)-1]$, that is, $r(j)=r(i)-1$.

Theorem 3.1. *Given CT-MC $\{Q\}$ under perturbation $(i,j)\rightsquigarrow(i,j')$ with $j\in\mathrm{R}[l(i)-1]$, it is robustly α-stable if and only if*

$$j'\in\mathbb{O}(i,j)^c, \tag{9}$$

where $\mathbb{O}(i,j):=\big\{k\in\mathscr{D}_n\mid\mathrm{Col}_k\big(\mathbb{R}(i,j)\big)\in\mathrm{null}\big(\mathbf{r}(i)\big)\big\}$ with $\mathrm{Col}_k(\cdot)$ being the kth column of the argument matrix.

Proof. Under perturbation $(i,j)\rightsquigarrow(i,j')$ with $l(j)=l(i)-1$, there are two possible positions for j': one is $l(j')\le l(i)$ (illustrated in Case 1 of FIGURE 1); the other is $l(j')>l(i)$ (illustrated in Cases 2 and 3 of FIGURE 1).

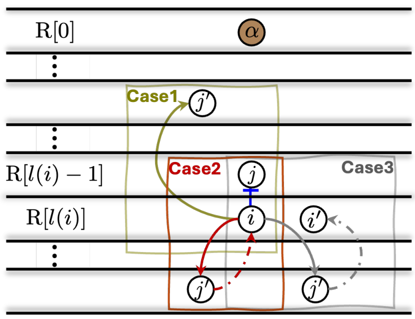


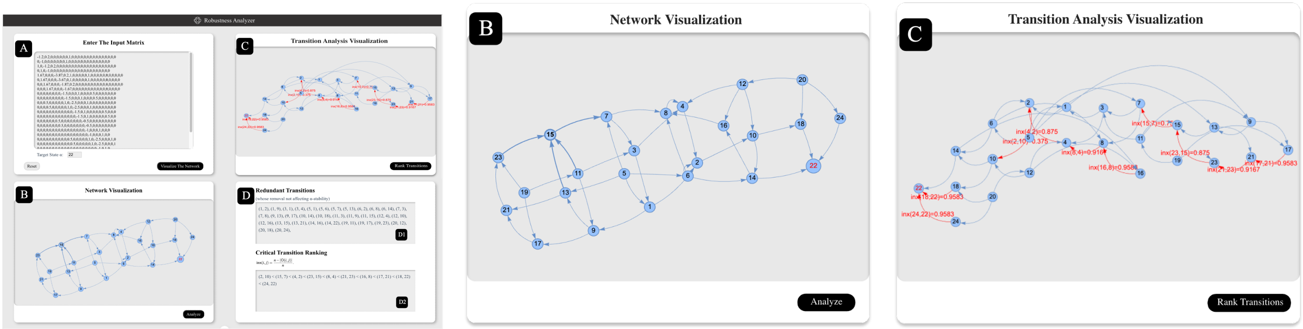
FIGURE 1. Three cases of perturbation $(i,j)\rightsquigarrow(i,j')$.

First, we prove the sufficiency by assuming $j'\in\mathbb{O}(i,j)^c$, which implies

$$j'\in\Big\{k\in\mathscr{D}_n\mid\big\langle\mathbf{r}(i),\mathrm{Col}_k\big(\mathbb{R}(i,j)\big)\big\rangle\ne0\Big\}.$$

If $i\in\mathbb{O}(i,j)^c$, meaning $\mathbf{r}(i)\cdot\mathrm{Col}_i\big(\mathbb{R}(i,j)\big)\ne0$, then one has $j'\in\bigcup_{r=0}^{l(i)}\mathrm{R}[r]\backslash\{i\}$ and $\big(Q-\Delta Q(i,j)\big)_{j',i}>0$ as in Case 1 of FIGURE 1. It implies the existence of a directed path from j' to α. If $i\in\mathbb{O}(i,j)$ but $j'\in\mathbb{O}(i,j)^c$, then there exists a state $i'\in\bigcup_{r=0}^{l(i)}\mathrm{R}[r]\backslash\{i\}$ such that $\Big[\sum_{l=1}^{L^\star-\|\mathbf{r}(i)\|_0-1}(Q-\Delta Q(i,j))^l\Big]_{i',j'}>0$ and $\Big[\sum_{l=1}^{l(i')}(Q-\Delta Q(i,j))^l\Big]_{\alpha,i'}>0$. Indicatively, there exists a directed path from i to j', then to i', and finally to α, with a length less than $L^\star-\|\mathbf{r}(i)\|_0+l(i')$, as illustrated in Case 3 of FIGURE 1. As a result, the robust α-stability is achieved.

Next, the necessity is proved by contradiction. Assume that



(a) Interface overview (b) Network visualization (c) Transition analysis visualization

FIGURE 2. Robustness Analyzer consists of four main regions. The Input Matrix Region (A) allows users to input the transition rate matrix, with the target state α specified, along with buttons to visualize the graph or reset the interface. Network Visualization Region (B) displays the network structure. When the 'Analyze' button is clicked, Transition Analysis Visualization Region (C) highlights the critical transitions in red with their robustness indicator values labeled. Upon clicking 'Rank Transitions', Redundant Transitions Region (D1) shows the transitions with the indicator value below 1, while Critical Transitions Ranking Region (D2) lists the remaining transitions sorted by their indicator values in ascending order.

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this CT-MC $\{Q\}$ is robustly α-stable but $j' \in \mathbb{O}(i,j)$. Note that

$$\begin{aligned}\mathbb{O}(i,j) &= \left\{k \in \mathscr{D}_n \mid \mathbf{r}(i)\cdot \mathrm{Col}_k\left(\mathbb{R}(i,j)\right) = 0\right\}\\ &= \left\{k \in \mathscr{D}_n \mid \mathbf{r}(i)\cdot \mathrm{Col}_k\left(Q-\Delta Q(i,j)\right)^{n-l} = 0, \forall l \in [0, \|\mathbf{r}(i)\|_0]\right\}.\end{aligned}$$

Let the sequence of the states succeeding i be given by $j_0 = i \to j_1 \to \cdots \to j_k \to \cdots \to j_{\|\mathbf{r}(i)\|_0}$, where

$$j_k \in \left\{\varsigma \in \mathscr{D}_n \mid e_{\varsigma,n}^{\top}\mathrm{Col}_i\left(Q-\Delta Q(i,j)\right)^k > 0\right\}, k \in [0, |\mathbb{O}(i,j)|].$$

It indicates the existence of subset $\mathbb{O}(i,j) \in \bigcup_{r=l(i)+1}^{L^\star} \mathrm{R}[r] \cup \{i\}$ such that $j_k \in \mathbb{O}(i,j)$ for all $k \in [0, |\mathbb{O}(i,j)|]$, as Case 2 in FIGURE 1. Consequently, we have

$$\lim_{t\to+\infty} \Pr\{x(t;j_k) \in \mathbb{O}(i,j)\} = 1,\ \forall\ j_k \in \mathbb{O}(i,j). \qquad (10)$$

Thus, according to Definition 2.2, the perturbed CT-MC $\{Q'\}$ cannot be asymptotically stable to α. Consequently, the original CT-MC $\{Q\}$ is not robustly α-stable, leading to a contradiction. Therefore, the proof is complete. □

Clearly, when $\mathbb{O}(i,j) \neq \emptyset$, perturbations to (i,j) are possible to destabilize this CT-MC $\{Q\}$. In contrast, when $\mathbb{O}(i,j) = \emptyset$, this CT-MC $\{Q\}$ achieves robust α-stability against arbitrary perturbations of the form $(i,j) \rightsquigarrow (i,j')$. Therefore, we obtain the following proposition.

Proposition 3.1. *CT-MC $\{Q\}$ is robustly α-stable under perturbation on (i,j) if and only if*

$$\mathrm{null}\left(\mathbf{r}(i)\right) \cap \mathrm{Col}\left(\mathbb{R}(i,j)\right) = \emptyset. \qquad (11)$$

Remark 3.1. *If $\mathbb{O}(i,j) = \bigcup_{r=l(i)+1}^{L^\star} \mathrm{R}[r] \cup \{i\}$, the state transition (i,j) acts as a bridge connecting two regions: one rooted at i and the other rooted at α. If we replace (i,j) with (i,j'), we may sever the connection between these two regions, thus isolating α from the influence of i. This disconnect can lead to a loss of stability, as the path to α is compromised.*

4. Robustness Assessment

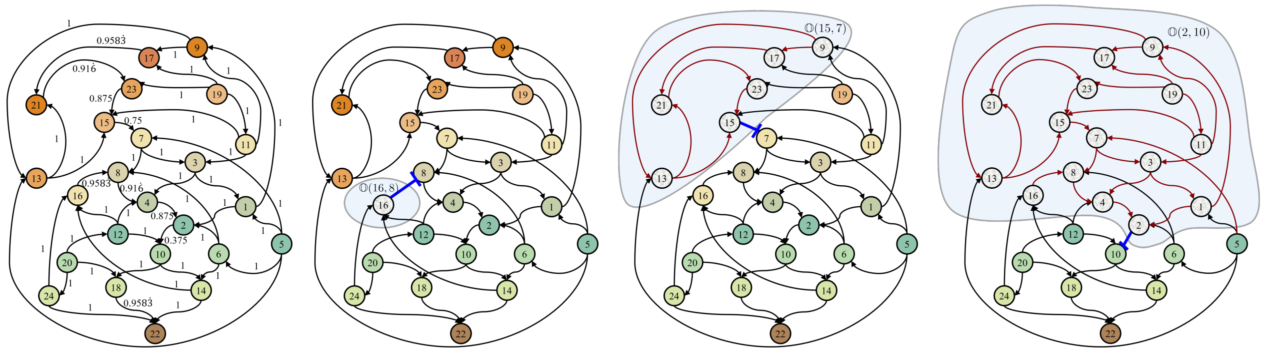
In this section, we quantitatively estimate the robustness of a given CT-MC $\{Q\}$. According to Proposition 3.1, the robust α-stability of CT-MC $\{Q\}$ is guaranteed if condition (11) holds for all $i \in \mathscr{D}_n$. Otherwise, it is crucial to assess the importance of each transition $(i,j) \in \mathscr{G}$, as the removal of any such transition could undermine the robust α-stability of CT-MC $\{Q\}$.

To proceed, we introduce a robustness indicator for transition $(i,j) \in \mathscr{G}$ as follows:

$$\mathrm{inx}(i,j) = \frac{n - |\mathbb{O}(i,j)|}{n}. \qquad (12)$$

A larger value of $\mathrm{inx}(i,j)$ indicates a higher robustness of the transition (i,j). In particular, if $\mathbb{O}(i,j) = \emptyset$, one has $\mathrm{inx}(i,j) = 1$, implying that the perturbation on (i,j) will not affect the α-stability of CT-MC $\{Q\}$.

Based on the above theoretical results, we can develop a network robustness analyzer, illustrated by an interactive visualization interface as FIGURE 2(a). By entering the network, the embedded algorithms within the interface will visualize the results of the robustness analysis.



(a) Robustness indicator (b) Critical transition $(16,8)$ (c) Critical transition $(15,7)$ (d) Critical transition $(2,10)$

FIGURE 3. TRG of p53-Mdm2 Signaling Model.

5. Illustrative Example: p53-Mdm2 Signaling

Here, we conduct a robustness analysis of the model for the p53 gene response to DNA damage, known as the p53-Mdm2 signaling network [5]. This logic model consists of four variables: p53 $\in \{0,1,2\}$, Mdm2C $\in \{0,1\}$, Mdm2N $\in \{0,1\}$, and Dam $\in \{0,1\}$. According to [3, 14], the transition graph of the p53-Mdm2 signaling network has 24 states, as illustrated in FIGURE 3(a), with each state represented by

$$x = 8(2-\text{p53}) + 4(1-\text{Mdm2C}) + 2(1-\text{Mdm2N}) + (1-\text{Dam}).$$

Especially, state 22 serves as the target state, indicating the situation where nuclear Mdm2 is on while the rest are off.

In this setting, 22-reachable sets can be calculated as follows:

$$\begin{gathered}\mathrm{R}[0]=\{22\};\ \mathrm{R}[1]=\{14,18,24\};\ \mathrm{R}[2]=\{6,10,20\};\\ \mathrm{R}[3]=\{2,5,12\};\ \mathrm{R}[4]=\{1,4\};\ \mathrm{R}[5]=\{3,8\};\\ \mathrm{R}[6]=\{7,11,16\};\ \mathrm{R}[7]=\{15,19\};\ \mathrm{R}[8]=\{13,23\};\\ \mathrm{R}[9]=\{9,21\};\ \mathrm{R}[10]=\{17\}.\end{gathered}$$

States within the same reachable set are represented in the same color in FIGURE 3(a). In this case, $L^\star = 10$. Next, according to Theorem 3.1, we calculate the invariant subset $\mathbb{O}(i,j)$ for $i \in \mathscr{D}_{24}\backslash\{22\}$ and $j \in \mathrm{R}[l(i)-1]$ as recorded in TABLE 1.

Next, we consider the perturbation on transition $(16,8)$, which represents a critical transition since $\mathbb{O}(16,8) = \{16\} \neq \emptyset$ as shown in FIGURE 3(b). According to Theorem 3.1, with $\alpha = 22$ here, if $j' \neq 16$, the resulting CT-MC $\{Q'\}$ achieves 22-stability. Conversely, if $j' = 16$, the resulting CT-MC $\{Q'\}$ fails to achieve 22-stability, indicating that the original CT-MC $\{Q\}$ is not robustly 22-stable under perturbation $(16,8) \rightsquigarrow (16,16)$. Furthermore, we examine the perturbation on transition $(15,7)$.

TABLE 1. Invariant state subset $\mathbb{O}(i,j)$ in state set $\bigcup_{r=l(i)+1}^{L^\star} \mathrm{R}[r] \cup \{i\}$.

(i,j)	$\mathbb{O}(i,j)$	(i,j)	$\mathbb{O}(i,j)$	(i,j)	$\mathbb{O}(i,j)$	(i,j)	$\mathbb{O}(i,j)$
$(24,16)$	$\emptyset$	$(24,22)$	$\emptyset$	$(18,22)$	$\{18\}$	$(14,16)$	$\emptyset$
$(14,22)$	$\emptyset$	$(20,24)$	$\emptyset$	$(20,18)$	$\emptyset$	$(20,12)$	$\emptyset$
$(10,18)$	$\emptyset$	$(10,14)$	$\emptyset$	$(6,2)$	$\emptyset$	$(6,8)$	$\emptyset$
$(6,14)$	$\emptyset$	$(2,10)$	$\{1,2,4,7,8,9,11,13,$ $15,16,17,19,21,23\}$	$(12,4)$	$\emptyset$	$(12,10)$	$\emptyset$
$(12,16)$	$\emptyset$	$(5,1)$	$\emptyset$	$(5,6)$	$\emptyset$	$(5,7)$	$\emptyset$
$(5,13)$	$\emptyset$	$(1,2)$	$\emptyset$	$(1,9)$	$\emptyset$	$(4,2)$	$\{4,8,16\}$
$(3,1)$	$\emptyset$	$(3,4)$	$\emptyset$	$(8,4)$	$\{8,16\}$	$(16,8)$	$\{16\}$
$(7,3)$	$\emptyset$	$(7,8)$	$\emptyset$	$(11,3)$	$\emptyset$	$(11,9)$	$\emptyset$
$(11,15)$	$\emptyset$	$(15,7)$	$\{9,13,15,17,21,23\}$	$(19,11)$	$\emptyset$	$(19,17)$	$\emptyset$
$(19,23)$	$\emptyset$	$(23,15)$	$\{9,17,21\}$	$(13,15)$	$\emptyset$	$(13,21)$	$\emptyset$
$(9,17)$	$\emptyset$	$(9,13)$	$\emptyset$	$(21,23)$	$\{17,21\}$	$(17,21)$	$\{17\}$

As can be seen from FIGURE 3(c), if $j' \in \mathbb{O}(15,7)$, the stability of CT-MC $\{Q\}$ will be compromised; otherwise, the stability will be maintained. Finally, we analyze the most severe case where the transition $(2,10)$ is perturbed. As shown in FIGURE 3(d), if $j' \in \mathbb{O}(2,10)$, the reachability from states in $\mathbb{O}(2,10)$ to states in $\mathscr{D}_{24}\backslash\mathbb{O}(2,10)$ will be lost, leading to the instability of CT-MC $\{Q\}$. This phenomenon corroborates the scenario mentioned in Remark 3.1, demonstrating that transition $(2,10)$ acts as a bridge. Besides, it reveals that the larger the invariant state set $\mathbb{O}(i,j)$, the greater the possibility that the perturbation on the transition (i,j) will affect the stability of CT-MC $\{Q\}$.

To assess the criticality of transition perturbations, we calculate the robustness indicator for each transition $(i,j) \in \mathscr{G}$, as annotated on the arcs in FIGURE 3(a). For example, we consider the case of perturbing transition $(3,4)$. This yields $\mathbf{r}(3) = (1,1,0,0,1,1,0,0,0,1,0,1,0,1,0,0,0,1,0,1,0,1,0,1)$ and $\mathbb{R}(3,4) = \sum_{l=1}^{13}\left(Q + \Delta Q(3,4)\right)^l$, which results in

$$\text{null}\big(\mathbf{r}(3)\big) \cap \text{Col}\big(\mathbb{R}(3,4)\big) = \emptyset.$$

According to Proposition 3.1, CT-MC $\{Q\}$ is robustly 22-stable under perturbation on $(3,4)$, consistent with the robustness indicator $\text{inx}(3,4) = 1$. As shown in FIGURE 3(a), transitions with higher $\text{inx}(i,j)$ values exhibit stronger robustness. Specifically, when $\text{inx}(i,j) = 1$, perturbation on transition (i,j) has no effect on the stability of CT-MC $\{Q\}$.

6. Conclusions

This paper has established a robust stability analysis framework for CT-MCs under transition perturbations, including the establishment of stability criteria and the formulation of robustness indicators. In particular, the robustness indicator has quantified the significance of each transition to system stability, allowing for the identification of critical transitions whose perturbations are most likely to destabilize the system. Finally, we have demonstrated the applicability of the framework through a case study on the p53-Mdm2 signaling network.

Acknowledgements

This work was partially supported by the National Natural Science Foundation of China (62273286), GRF (17200124), the Shenzhen-Hong Kong-Macau Technology Research Programme (SGDX20230821091559019), the Guangdong Basic Research and Applied Research Fund (2024A1515011509), the Research Grants Council of Hong Kong (STG1/E-401/23-N, C4026-21G, 17209021), the Australian Research Council (DP240101140), and the Innovation and Technology Commission of the HKSAR Government under the InnoHK initiative.

References

[1] J. B. Clempner and A. Poznyak, "Continuous-time Markov chains," in *Optimization and Games for Controllable Markov Chains: Numerical Methods with Application to Finance and Engineering*, pp. 65–84, Springer, 2023.

[2] K. Lange, "Continuous-time Markov chains," in *Applied Probability*, pp. 247–291, Springer, 2024.

[3] Y. Guo, Z. Li, Y. Liu, and W. Gui, "Asymptotical stability and stabilization of continuous-time probabilistic logic networks," *IEEE Transactions on Automatic Control*, vol. 67, no. 1, pp. 279–291, 2021.

[4] S. Zhu, Y. Li, J. Cao, G. M. Dimirovski, and J. Lu, "Lyapunov-type criteria of absorbing continuous-time Markov chains," *IEEE Transactions on Automatic Control*, vol. 69, no. 4, pp. 2422–2428, 2023.

[5] G. Stoll, E. Viara, E. Barillot, and L. Calzone, "Continuous time Boolean modeling for biological signaling: application of gillespie algorithm," *BMC Systems Biology*, vol. 6, pp. 1–18, 2012.

[6] J. Guang, Y. Xu, and J. Dai, "Steady-state convergence of the continuous-time routing system with general distributions in heavy traffic," *Proceedings of the ACM on Measurement and Analysis of Computing Systems*, vol. 9, no. 1, pp. 1–29, 2025.

[7] R. Zhang, M. V. Shah, J. Yang, S. B. Nyland, X. Liu, J. K. Yun, R. Albert, and T. P. Loughran Jr, "Network model of survival signaling in large granular lymphocyte leukemia," *Proceedings of the National Academy of Sciences*, vol. 105, no. 42, pp. 16308–16313, 2008.

[8] L. Lin, J. Lam, W.-K. Ching, Q. Qiu, L. Sun, and B. Min, "Finite-time stabilizers for large-scale stochastic Boolean networks," *IEEE Transactions on Cybernetics*, vol. 55, no. 5, pp. 2098–2109, 2025.

[9] S. Zhu, J. Cao, L. Lin, J. Lam, and S.-i. Azuma, "Toward stabilizable large-scale Boolean networks by controlling the minimal set of nodes," *IEEE Transactions on Automatic Control*, vol. 69, no. 1, pp. 174–188, 2023.

[10] Y. Xiao and E. R. Dougherty, "The impact of function perturbations in Boolean networks," *Bioinformatics*, vol. 23, no. 10, pp. 1265–1273, 2007.

[11] L. Lin, J. Lam, P. Shi, M. K. Ng, and H.-K. Lam, "Learning probabilistic logical control networks: From data to controllability and observability," *IEEE Transactions on Automatic Control*, vol. 70, no. 6, pp. 3889–3904, 2025.

[12] X. Li, H. Li, and G. Zhao, "Function perturbation impact on feedback stabilization of Boolean control networks," *IEEE Transactions on Neural Networks and Learning Systems*, vol. 30, no. 8, pp. 2548–2554, 2018.

[13] W. Li, H. Li, and X. Yang, "Robust stability of Boolean networks subject to edge perturbations," *IEEE Transactions on Systems, Man, and Cybernetics: Systems*, vol. 54, no. 9, pp. 5617–5626, 2024.

[14] W. Abou-Jaoudé, D. A. Ouattara, and M. Kaufman, "From structure to dynamics: frequency tuning in the p53–mdm2 network: I. logical approach," *Journal of Theoretical Biology*, vol. 258, no. 4, pp. 561–577, 2009.