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On the Geometry of Chemical Reaction Networks:
Lyapunov Function and Large Deviations

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To Herbert, Jürg, and Tom, friends and inspirations.

Abstract In an earlier paper, we proved the validity of large deviations theory for the particle approximation of quite general chemical reaction networks (CRNs). In this paper, we present a more geometric insight into the mechanism of that proof, exploiting the notion of spherical image of the reaction polytope. This allows to view the asymptotic behavior of the vector field describing the mass-action dynamics of chemical reactions as the result of an interaction between the faces of this polytope in different dimensions. We also illustrate some local aspects of the problem in a discussion of Wentzell-Freidlin (WF) theory, together with some examples.

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1 Introduction

The aim of this paper is to give some more contextual explanations concerning our paper [1]. That paper dealt with large deviation theory for the particle approximation of chemical reaction networks. After introducing the setup of [1], we expand the presentation by several examples which illustrate the difficulties of finding adequate conditions for the large deviation principle to hold on the full phase space. Furthermore, we also present a more geometrical proof of the so-called “toric jet” method [17] used in [11]. We will see that the geometric method, while similar in spirit to the work of [17], exhibits the simple geometric ideas which concern the asymptotic nature of ODE’s with polynomial nonlinearities.

Modeling the dynamics of large sets of chemical reactions has gained interest in recent years thanks to the increased amount of biological data on complex chemical systems. These dynamics take place in high dimensional spaces (with dimension equal to the number of species involved in the chemical reactions) and display highly complex dynamical behavior (all classes of attractors can be realized by models of chemical reaction systems [24,27]). The theoretical study of such dynamics is a topic of central interest in domains such as chemical reaction network theory [13,21] and, more generally, systems biology, dedicated to the understanding of the laws governing large scale biochemical systems. Progress in this direction can be made by considering stochastic effects in chemical systems. Indeed, as is the case in equilibrium statistical mechanics, large fluctuations induce transitions between the different attractors of the system, whose state finally stabilizes, in the probabilistic sense, in a neighborhood of the (in general) unique attractor with the lowest potential energy. In this sense, stochastic models and their probabilistic distribution (or the evolution of their stochastic paths) are ideal for studying the short and long term-behavior of complex biochemical systems. Indeed, the mathematical study of stochastic chemical dynamics has been an active area of research already at the end of last century [12]. Recently, probability distributions for CRNs in detailed balance have been fully characterized through an analogy with Jackson Networks in [4]. The steady states of such systems are equilibrium states and are unique for every invariant manifold of the dynamical system [13,19]. However, many systems of practical interest in cell biology fall in the category of nonequilibrium systems, whose study is still an open topic even at the fundamental level [31].

One promising tool for the systematic study of the stochastic dynamics of such nonequilibrium systems is potential landscape theory for chemical reaction systems, and more generally for biochemical systems. This theory has recently been investigated in, e.g., [35]. Here a large deviations rate function from WF theory (called the WF quasipotential) has been indicated as a promising candidate for a potential landscape function. However, the intuition developed in [35] is not always rigorously justifiable in the case of mass action systems. In particular, the WKB approximation used for the derivation of the Hamilton Jacobi Equation (HJE) for the WF potential is not guaranteed to converge, and a rigorous framework for infinite-dimensional integration in the space of paths has not yet been established. Moreover, it is well known [15,32] that for mass action systems the diffusion processes studied in [35] are large-volume approximations of the microscopically justified Markov jump models and that the potential landscapes predicted by WF theory differ in these two processes.
In this article, we initiate a formal study of potential landscape theory for Markov jump models of CRNS with mass action kinetics in the large volume limit through the rigorous establishment of estimates à la WF. Markov jump models are the framework of choice for the modeling of the dynamics of CRNS because they embody the discrete character of the interacting particles at the microscopic level. Such processes can then be scaled [4,12,29] to study the behavior of large amounts of reacting molecules by considering reactors with volume $v$ and taking $v$ as scaling parameter. The effect of this scaling on the model is a reduction of the amplitude of the stochastic fluctuations in phase space. The study of fluctuations in finite time of stochastic systems in the large volume limit is the object of large deviations theory [10]. The exponential estimates obtained with this theory can be extended to infinite time intervals through WF theory, allowing in particular to give exponential estimates of exit times from compact sets in phase space, transition times between different attractors and invariant measure densities. Furthermore, WF theory establishes a mathematically rigorous framework for potential landscape theory for biochemical systems through the definition of a quasipotential function $V(x)$. This quasipotential is one of the most promising candidates for the generalization of equilibrium potentials in statistical mechanics to nonequilibrium systems [31].

The paper is structured as follows. In the first section we introduce the reader to deterministic and stochastic mass action models for the dynamics of CRNS. We then outline some typical statements of large deviations theory with particular attention to problems in theoretical biochemistry. Appealing to the companion paper [1], we then introduce a class of CRNS for which the applicability of a large deviations principle (LDP) and ultimately WF estimates has been rigorously established. This class of CRNS (the strongly endotactic CRNS [17]) is characterized solely on the base of the topology of the underlying network of reactions and is therefore independent of reaction constants. This has the advantage of avoiding difficult estimates on the high-dimensional stochastic dynamics of the corresponding perturbed dynamical system. We also provide an alternative, constructive proof of geometric character of the results in [1]. This approach is somewhat related to tropical geometry [9]. Finally, we discuss the extension of large deviations estimates to the infinite time horizon through WF theory and give a dynamically nontrivial example of a CRN to which such results can be applied.

2 The model

We consider a set $S := \{s_1, \ldots, s_d\}$ of $d$ interacting chemical species. The transitions between different species are described by a set $R = \{r_1, \ldots, r_m\}$ of $m$ chemical reactions. Every reaction $r \in R$ can uniquely be written in the form

$$ r = \left\{ \sum_{i=1}^{d} (c^r_{\text{in}})_i s_i \rightarrow \sum_{i=1}^{d} (c^r_{\text{out}})_i s_i \right\}, $$

where the nonnegative integer vectors $c^r_{\text{in}}, c^r_{\text{out}}$ counting the species multiplicities as inputs and outputs of the reaction are called, respectively, the input and output complexes of $r$. We finally denote by $C := \{c^r_{\#} : r \in R, \# \in \{\text{“in”, “out”}\}\}$ the set of complexes, and for each $r$ we define a reaction vector

$$ c^r := c^r_{\text{out}} - c^r_{\text{in}}, $$

(2.1)
describing the net effect of $r$ on the system. A CRN is defined by the triple $(S, C, R)$.

**Remark 2.1.** We extend the definitions to include open chemical networks, by associating with sinks and external nonautocatalytic sources the complex zero vector (with $d$ components), denoted by $\emptyset$.

**Example A.** The system

$$A + 2B \xrightarrow{r_1} 3B$$

(2.2)

is a CRN with $S = \{A, B\}$ and $R = \{r_1, r_2\}$. The set of complexes of this reaction is $C = \{\{A + 2B\}, \{3B\}\} = \{(1, 2), (0, 3)\}$ (in the basis spanned by $(A, B)$).

### 2.1 Deterministic mass action kinetics

The state of the system is described by the *vector of concentrations* $x \in \mathbb{R}^d_+$ (the set of $d$-dimensional nonnegative reals) of the $d$ species. Its evolution is commonly described by the *mass action kinetics* model, which is the set of ODES

$$\frac{dx}{dt} = \sum_{r \in R} \lambda_r(x) e^r,$$

(2.3)

where $\lambda$ is the monomial

$$\lambda_r(x) := k_r \prod_{i=1}^d c_i^{x_i},$$

(2.4)

describing the reaction rate of reaction $r$. The constants $\{k_r\} \in (0, \infty)$ are called reaction rate constants.

**Remark 2.2.** Note that the set $\mathbb{R}^d_+$ is invariant under the dynamics described by (2.3): For every $s_i \in S$, any reaction $r \in R$ reducing the amount of $s_i$ in the reactor will have $(c_i^{x_i})_r > 0$, implying by (2.4) that $\lambda_r(x) = 0$ on $\{x \in \mathbb{R}^d_+ : x_i = 0\}$. Furthermore, again by (2.3), for each initial condition $x_0 \in \mathbb{R}^d_+$, $x(t)$ remains in $S_{x_0} := (x_0 + \text{span}\{e^r : r \in R\}) \cap \mathbb{R}^d_+$. This space is called the stoichiometric compatibility class of $x_0$ and can be less than $\mathbb{R}^d_+$.

**Example A.** The time derivative of a trajectory $x(t)$ for Network (2.2) is given by

$$\frac{dx}{dt} = k_1 \lambda_{r_1}(x) e^{r_1} + k_2 \lambda_{r_2}(x) e^{r_2} = k_1 x_A x_B^2 \begin{pmatrix} -1 \\ 1 \end{pmatrix} + k_2 x_B^3 \begin{pmatrix} 1 \\ -1 \end{pmatrix},$$

for reaction rate constants $k_1, k_2 \in (0, \infty)$. A trajectory starting at $x_0 \in \mathbb{R}^2_+$ cannot leave the stoichiometric compatibility class

$$S_{x_0} = \left\{ x_0 + \text{span} \begin{pmatrix} -1 \\ 1 \end{pmatrix} \right\} \cap \mathbb{R}^2_+. $$
Example B. Consider the (open) CRN

\[ 0 \xrightarrow{k_1} A + 2B \xrightarrow{k_2} 3B \xrightarrow{k_3} A. \]  

(2.5)

The dynamics of this CRN is described by the solution \( x(t) \) of the equation

\[ \frac{dx}{dt} = k_1 \left( \frac{1}{2} \right) + k_2 x_A x_B^2 \left( -1 \right) + k_3 x_B^3 \left( \frac{1}{-3} \right), \]  

(2.6)

where \( x_A \) and \( x_B \) are the concentrations of \( A \) and \( B \) respectively. Fig. 1 represents the vector field of (2.6). In this case the stoichiometric compatibility class of the network is \( S_{x_0} = \mathbb{R}^2_+ \) for all \( x_0 \in \mathbb{R}^2_+ \).

2.2 Stochastic mass action kinetics

We now replace the ODE by a stochastic process, which appears when one takes into account that chemical reactions are formed by a discrete set of molecules. We are interested in the approximation of perfect mixing, i.e., we only consider numbers of molecules, but not their spatial distribution. This is then a mean field pure jump Markov process \([12]\) whose central object is the random vector \( N_t \in \mathbb{N}_0^d \) (the set of \( d \)-dimensional nonnegative integers), representing the number of molecules of the \( d \) species at time \( t \). Every reaction \( r \in \mathcal{R} \) describes a possible jump of the process \( N_t \) as a transition

\[ N_t \rightarrow N_t + e^r, \]
where $c^r$ is the reaction vector associated with $r \in \mathcal{R}$ as defined in (2.1).

The state-dependent mean field rate $A_r(N_t)$ of jumps of the process $N_t$ in direction $c^r$ under mass action kinetics is then proportional to the number of unordered configurations of the (distinguishable) molecules and is modeled as

$$A_r(N_t) = k_r \prod_{i=1}^{d} \binom{N_t}{c^r_n} (c^r_n)_i!,$$

(2.7)

where $k_r$ is the reaction rate constant of reaction $r$. The generator $L$ of the process is

$$L_f(N_t) = \sum_{r \in \mathcal{R}} A_r(N_t) (f(N_t + c^r) - f(N_t)) .$$

(2.8)

We are interested in the scaling of the dynamics of the system for large volumes, i.e., as we increase the number of particles by a large multiplicative factor. We denote by $v$ the volume of the system under consideration and we define the vector of concentrations $X_v$ as the linear scaling of $N_t$ in $v$, i.e.,

$$X_v^v := v^{-1} N_t .$$

(2.9)

The natural scaling in volume $v$ of the reaction rate constants is

$$k^{(v)}_r := v^{-\|c^r_n\|_1} k_r ,$$

(2.10)

where $\| \cdot \|_1$ is the 1-norm in $\mathbb{R}^d$. This results in extensive laws for the reaction rates, appearing in the generator of the scaled process $X_v^v$:

$$L_v f(x) := v \sum_{r \in \mathcal{R}} A_{r,v}(x) \left( f(x + v^{-1} c^r) - f(x) \right) , \quad x \in (v^{-1} \mathbb{N}_0)^d ,$$

(2.11)

where we define

$$A_{r,v}(x) = k^{(v)}_r \prod_{i=1}^{d} \binom{v x_i}{c^r_n} (c^r_n)_i! = \lambda_r(x) + o_v(1) \quad \text{as } v \to \infty .$$

(2.12)

For a fixed volume $v$ it follows that the phase space of $X_v^v$ is $(v^{-1} \mathbb{N}_0)^d$. In general, this process is not irreducible, as the set of possible transitions of $X_v^v$ might not reach every point in phase space (e.g., a reaction might map even numbers of species only on even numbers).

It is well known [12] that for any time $T > 0$, in the limit $v \to \infty$ the sample paths of the process $X_v^v$ with initial condition $\lim_{v \to \infty} X_v^v = x_0 \in \mathbb{R}_+^d$ converge almost surely on $[0, T]$ towards the solution of the odes (2.3) starting at $x_0$, provided that such a solution exists on $[0, T]$. This extends to strong convergence through the establishment of a Central Limit Theorem for the trajectories of $X_v^v$ [12].
3 Large deviations theory

We now study the v-approximation in the context of large deviations theory to estimate the probabilities of finding paths which deviate from the deterministic model \([10,29]\). This will allow to establish exponential tail estimates on the probability measure in the space of paths. In our case, by the jumping nature of the process \(X^v_t\), this space is the Skorokhod space, i.e., the space of functions that are everywhere right continuous and having left limits (also called càdlàg functions). Throughout, we denote by \(D_{0,T}(\mathbb{R}^d_+)\) the Skorokhod space, or space of càdlàg functions \(z : [0,T] \to \mathbb{R}^d_+\), equipped with the topology of uniform convergence.

In this space, the typical statement of large deviations theory is summarized in the following definition from [10].

**Definition 3.1.** Fix \(T\) finite and a lower semi-continuous mapping \(I : D_{0,T}(\mathbb{R}^d_+) \to [0, \infty]\) such that for any \(\alpha \in \mathbb{R}^+\), the level set \(\{z : I(z) \leq \alpha\}\) is a compact subset of \(D_{0,T}(\mathbb{R}^d_+)\). The probability distribution of sample paths of the process \(\{X^v_t\}_{v \in \mathbb{N}}\) with fixed initial condition \(X^v_0 \to x \in \mathbb{R}^d_+\) obeys a Large Deviations Principle (LDP) with good rate function \(I(\cdot)\) if for any measurable \(\Gamma \subset D_{0,T}(\mathbb{R}^d_+)\) we have

\[
\begin{align*}
- \inf_{z \in \bar{\Gamma}} I(z) &\leq \liminf_{v \to \infty} \frac{1}{v} \log \mathbb{P}_{X^v_0} \left[ X^v_t \in \Gamma \right] \\
&\leq \limsup_{v \to \infty} \frac{1}{v} \log \mathbb{P}_{X^v_0} \left[ X^v_t \in \bar{\Gamma} \right] \leq - \inf_{z \in \bar{\Gamma}} I(z),
\end{align*}
\]

(3.1)

where \(\Gamma, \bar{\Gamma}\) denote the interior and the closure of the set \(\Gamma\) respectively.

In the case of pure jump Markov processes, it is well known [29] that a candidate for a good rate function can be obtained by analogy with the theory of Lagrangian mechanics. Indeed, by defining the Lagrangian function

\[
L(\lambda, \xi) = \sup_{\varrho \in \mathbb{R}^d} \left\{ \langle \varrho, \xi \rangle - \sum_{r \in \mathcal{R}} \lambda_r \left[ \exp(\langle \varrho, c^r \rangle) - 1 \right] \right\},
\]

one defines the rate function \(I_{x_0,T}\) for fixed \(x_0, T < \infty\) as the corresponding action along a path \(z \in D_{0,T}(\mathbb{R}^d_+)\), i.e.,

\[
I_{x_0,T}(z) = \begin{cases} 
\int_0^T L(\lambda(z), \dot{z}) \, dt & \text{if } z \in AC_{0,T}(\mathbb{R}^d_+), \, z(0) = x_0 \\
\infty & \text{otherwise}
\end{cases}
\]

(3.2)

where \(AC_{0,T}(\mathbb{R}^d_+)\) is the set of absolutely continuous paths \(z : [0,T] \to \mathbb{R}^d_+\). Continuing the analogy with Lagrangian mechanics, the LDP expressed in (3.1) corresponds to the minimum action principle, and more precisely with the path integral formulation of quantum mechanics stated in rigorous probabilistic terms.

Standard large deviations tools allow us to deduce (see [29]) that the sample paths of process \(X^v_t\) obey a LDP with the rate functions of (3.2) under the following

**Condition 3.2.** The rates \(\lambda_r : \mathbb{R}^d_+ \to \mathbb{R}\) are, on \(\mathbb{R}^d_+\),

(0) uniformly bounded away from 0, and
In the framework of stochastic mass action kinetics, Condition 3.2 is in general not satisfied. Indeed, neither the reaction rates $\Lambda_{r,v}$ are in general bounded away from zero (see Remark 2.2) nor are they uniformly Lipschitz continuous on $(\nu^{-1}\mathbb{N}_0)^d$, as can be verified by inspection of (2.12).

Condition 3.2 (0) guarantees the nondegeneracy of $X_v^t$ within $S_{x_0}$, whereas Condition 3.2 ($\infty$) is used in this framework to ensure that the process leaves a certain, large, compact with a probability that is negligibly low at the exponential scales of our estimates. While Condition 3.2 fails for general CRNs, we show directly that the LDP (3.1) holds for a large class of CRNs, which we will call ASE. To this end, we require the following more technical definition.

**Definition 3.3.** The process $X_v^t$ satisfies an exponential compact containment condition if there is, for every $\alpha$, $\gamma$, $T < \infty$ a finite $\varrho_{\alpha,\gamma,T}$, so that

$$\limsup_{v \to \infty} \frac{1}{v} \log \left( \sup_{\|x_0\|_1 \leq \gamma} \mathbb{P}_{x_0} \left[ \sup_{t \in [0,T]} \|X_v^t\|_1 > \varrho_{\alpha,\gamma,T} \right] \right) \leq -\alpha. \quad (3.3)$$

**Remark 3.4.** Even though Def. 3.3 does not directly guarantee that the process $X_v^t$ is exponentially tight in $D_{0,T}([0,T], \mathbb{R}^d)$, such exponential tightness of $X_v^t$ can be proved by application of the Arzela-Ascoli theorem to the continuous process $\tilde{X}^t_v$ obtained by linearly interpolating the sample paths of $X_v^t$ between its jumps. As $\tilde{X}^t_v$ is exponentially equivalent [10] to $X_v^t$, the result carries over to the original process.

As demonstrated in our next example, Condition 3.2 ($\infty$) is not necessary for (3.3) in the class of models under consideration.

**Example C.** The CRN $2A \rightleftharpoons 3A$ clearly does not satisfy condition (3.3). Indeed, setting WLOG $k_1 = k_2 = 1$, the solution of the postasymptotic ODE $\dot{x}_A = x_A^2$ diverges at $T_{\infty}(x_0) < \infty$. Hence, for any $\varrho$ the LHS of (3.3) goes to 0 for $T \geq T_{\infty}(x_0)$.

There are of course CRNs which do not even satisfy (3.3).

**Example 3.5.** The CRN $2A \rightarrow 3A$ clearly does not satisfy condition (3.3). Indeed, setting WLOG the reaction rate constant $k = 1$, the solution of the postasymptotic ODE $\dot{x}_A = x_A^2$ diverges at $T_{\infty}(x_0) < \infty$. Hence, for any $\varrho$ the LHS of (3.3) goes to 0 for $T \geq T_{\infty}(x_0)$.

Working via the compact containment of Def. 3.3 we show in [11] that Condition 3.2 can be relaxed, so the LDP (3.1) holds under the following assumption about the existence of a suitable Lyapunov function $U(\cdot)$. 

($\infty$) uniformly Lipschitz continuous.
Assumption A.1 (H, Ass. A.1). Let $X_v^t$ be the solution of the martingale problem generated by $\mathcal{L}_v$ of (2.11). We assume

(a) There exists a $b < \infty$ such that for all $\varrho > 0$ one can find a $\varrho^*(\varrho)$ such that for all $v > \varrho^*$ when $x \in (v^{-1}\mathbb{N}_0)^d$, 
\[
(\mathcal{L}_v U^v(x)) \leq e^{b v},
\]
where $U^v$ represents the $v$-th power of $U$.

(b) The Markov chain associated to $X_v^t$ reaches a state $x_+^\varrho$ in the strictly positive orthant $(v^{-1}\mathbb{N})^d$ with positive probability.

Assumption A.1 is satisfied by the network in Example C (continued). Defining $U(x) := e^x$ we have that
\[
\mathcal{L}_v U^v(x) = v A_1^{(v)}(x) (e^{v x - 2} - e^{v x}) + v A_2^{(v)}(x) (e^{v x + 2} - e^{v x})
= ve^{v x(v x - 1)}(e^{-2} - 1) + (e^{2} - 1) < 0,
\]
when $x > A/v$, thereby proving that this system satisfies Assumption A.1 (a). Assumption A.1 (b) is also trivially satisfied by the existence of the reaction $\emptyset \twoheadrightarrow 2 A$.

Remark 3.8. Assumption A.1 implies that the ODEs (2.3) have a global solution, as shown in H.

4 Topological conditions

In concrete applications, e.g., in biochemistry where typically $d \sim 100$, establishing estimates such as (3.3) can be particularly challenging. For this reason, in H a large class of networks has been shown to automatically verify the conditions in Assumption A.1. We illustrate next the ideas behind these conditions. By definition (2.4), some of the jump rates of $X_v^t$ vanish at the boundaries of phase space (i.e., where the concentration of some of the species vanishes). This implies that on those boundaries the vanishing reactions will be canceled from the network $(\mathcal{S}, \mathcal{C}, \mathcal{R})$, making the dynamics there qualitatively different from the one in the bulk $(\mathbb{R}_+^d)^\circ$. To take this into account, the definitions introduced next have boundary-specific character.

For the chemical ODE, an orbit cannot end on a boundary in finite time if it has started in the interior of the positive orthant of concentrations. But for the discrete particle approximation in finite volume, a species might disappear with finite (albeit small) probability. If there is no reaction which re-creates this species, the system gets stuck in there, and the large deviation principle fails in the sense that ergodicity is broken. Therefore, for our results to hold, we need criteria on chemical networks which guarantee that this “sticking” does not happen. As this sticking could happen also with several species at once, we need to define an exit condition from general subspaces (which we call $\mathcal{P}$, below). It will be seen that these exit conditions can be algorithmically verified.
We now proceed to define the necessary quantities for the study of configurations where some species are extinct. We classify $x \in (\mathbb{Z}_+)^d$ depending on its support, i.e., the set $\mathcal{P}$ of species that are present in strictly positive concentrations. Fixing $\mathcal{P} \subseteq \mathcal{S}$ with cardinality $d_\mathcal{P} := |\mathcal{P}|$, we denote by $\pi_\mathcal{P} : \mathbb{R}^d \to \mathbb{R}^{d_\mathcal{P}}$ the projection onto the coordinates with indices in $\mathcal{P}$. For any $w \in \mathbb{R}^{d_\mathcal{P}}$ and any set $\mathcal{A} \subset \mathbb{R}^{d_\mathcal{P}}$, we define the set $\mathcal{A}_w$ as the set of points in $\mathcal{A}$ that maximize the scalar product with $w$. We also denote by $\mathcal{R}(\mathcal{P})$ the set of reactions with inputs in $\mathcal{P}$ (i.e., $\text{supp} \ c^\mathcal{P}_\text{in} \subseteq \mathcal{P}$). For all $w \in \mathbb{R}^d$ with non-zero projection $w_\mathcal{P} := \pi_\mathcal{P} w$, we then let $\mathcal{R}(\mathcal{P})_w$ denote the reactions in $\mathcal{R}(\mathcal{P})$ maximizing the inner product $\langle w, c^\mathcal{P}_\text{in} \rangle$, i.e., those reactions corresponding to the elements of $\mathcal{C}_{\text{in}}(\mathcal{P})$ that are exposed by the vector $w$. Clearly, $\mathcal{R}(\mathcal{P})_w$ depends only on $w_\mathcal{P}$ which w.l.o.g is in the $(d_\mathcal{P} - 1)$-dimensional unit sphere $S^{d_\mathcal{P}-1}$. When $\mathcal{P} = \mathcal{S}$ we will write $\mathcal{R}_w$ instead of $\mathcal{R}(\mathcal{S})_w$.

**Definition 4.1** ([1] Def. 3.6). For any $w_\mathcal{P} \in S^{d_\mathcal{P}-1}$, we say that a reaction $r \in \mathcal{R}(\mathcal{P})$ is:

- $w$-dissipative if $\text{supp} \ c^\mathcal{P}_\text{out} \not\subseteq \mathcal{P}$ or if $\langle w_\mathcal{P}, \pi_\mathcal{P} c^r \rangle < 0$,
- $w$-null if $\text{supp} \ c^\mathcal{P}_\text{out} \subseteq \mathcal{P}$ and $\langle w_\mathcal{P}, \pi_\mathcal{P} c^r \rangle = 0$,
- $w$-explosive if $\text{supp} \ c^\mathcal{P}_\text{out} \not\subseteq \mathcal{P}$ and $\langle w_\mathcal{P}, \pi_\mathcal{P} c^r \rangle > 0$.

**Remark 4.2.** For $\mathcal{P} = \mathcal{S}$ our Def. 4.1 of $w$-dissipative and $w$-explosive reactions coincides with [17] Def. 6.15 of $w$-sustaining and $w$-draining reactions, respectively. The nomenclature was changed to stress the behavior of reactions for $\|x\|_1 \gg 1$: As we will see below, dissipative [explosive] reactions contribute to the decrease [increase] of a certain Lyapunov function $U(x)$ along trajectories far away from the origin.

**Definition 4.3** ([1] Def. 3.8). A CRN $(\mathcal{S}, \mathcal{C}, \mathcal{R}(\mathcal{P}))$ is called strongly $\mathcal{P}$-endotactic if the set $\mathcal{R}(\mathcal{P})_w$ contains at least one $w$-dissipative reaction, and no $w$-explosive reactions for any $w \in \mathbb{R}^d$ with non-zero projection onto $\mathcal{P}$ (or $w_\mathcal{P} \in S^{d_\mathcal{P}-1}$).

Finally, we say that a network is strongly endotactic if it is strongly $\mathcal{S}$-endotactic.

**Lemma 4.4** ([1] Lemma 3.9). If $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ is strongly $\mathcal{S}$-endotactic then for all $\mathcal{P} \subset \mathcal{S}$ with $\mathcal{R}(\mathcal{P}) \neq \emptyset$, $(\mathcal{S}, \mathcal{C}, \mathcal{R}(\mathcal{P}))$ is strongly $\mathcal{P}$-endotactic.

At this point we can introduce a visual representation of CRNs. A CRN $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ can be uniquely represented in $\mathbb{N}_0^d$ by drawing for each $r \in \mathcal{R}$ the vector $c^r$ starting at $c^\mathcal{P}_\text{in}$. We call this diagram the complex diagram of $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ and denote the convex hull of the set $c^\mathcal{P}_\text{in} := \{c^r : r \in \mathcal{R}\}$ by the complex polytope $\mathcal{W}$ of the network.

**Example B.** Consider the reaction network (2.5) described in Fig. 2. There are 3 faces:

\[ F_{13} := (3B, A + 2B), \quad F_{32} := (A + 2B, \emptyset), \quad F_{12} := (\emptyset, 3B), \]

and 3 reactions:

\[ r_1 := \{3B \to A\}, \quad r_2 := \{\emptyset \to A + 2B\}, \quad r_3 := \{A + 2B \to 3B\}. \]

One checks that for the normal $n_1$ to $F_{13}$, $\langle n_1, c^{r_1} \rangle < 0$, $\langle n_1, c^{r_3} \rangle = 0$ and $r_2$ is not considered because it does not originate in $F_{13}$. 

\[ n_1 = 3B, \quad n_2 = 2B, \quad n_3 = A + 2B, \quad n_4 = 3B. \]
Fig. 2: The complex diagram of network 2.5. The shaded region is the complex polytope of the network. A vector \( w \in \mathbb{R}^d \) has been drawn in red, together with its normal hyperplane, in order to identify the \( w \)-maximal subset of the input complexes \( C^w(S)_w \); The complex \( A + 2B \).

On the face \( F_{32} \) the scalar products are \( \langle n_2, c^{r_3} \rangle < 0 \), \( \langle n_2, c^{r_2} \rangle = 0 \), and \( r_1 \) need not be considered. Finally, we have \( \langle n_3, c^{r_1} \rangle < 0 \), \( \langle n_3, c^{r_2} \rangle < 0 \), and \( r_3 \) is not considered.

Thus, the system \( \emptyset \rightarrow A + 2B \rightarrow 3B \rightarrow A \) is strongly endotactic.

Example D. We give two examples of networks that do not meet some of the requirements of Def. 4.3.

Fig. 3: Complex diagrams of the CRNs in Example D (4.1) on the left and (4.2) on the right).

(a) The network

\[
\emptyset \rightarrow A + 2B \rightarrow 3B \rightarrow A \quad 2A \rightleftharpoons A + 3B \ , \quad (4.1)
\]

represented in Fig. 3 left, is not strongly endotactic. Indeed, taking \( n^* \) as the normal vector to the \( (A + 3B, 2A) \) face one sees that there is no reaction \( r \in \mathcal{R}_{n^*} \) with \( \langle n^*, c^r \rangle < 0 \).
(b) The network
\[ A \rightarrow 2A \rightarrow 3A + 2B \rightarrow A \] (4.2)
represented in Fig. 3 right, is strongly \( S \)-endotactic.

For \( \mathcal{P} = \{ A \} (S, C, \mathcal{R}(\mathcal{P})) \) is strongly \( \mathcal{P} \)-endotactic: For \( w_{\mathcal{P}} = (1) \in \mathbb{R}^1 \), the reaction \( r_+ = \{ 2A \rightarrow 3A + 3B \} \in \mathcal{R}(\mathcal{P})_{w_{\mathcal{P}}} \) is \( w_{\mathcal{P}} \)-dissipative (it has a positive component not in \( \mathcal{P} \)) and for \( w_{\mathcal{P}} = (-1) \) the reaction \( r_- = \{ A \rightarrow 2A \} \in \mathcal{R}(\mathcal{P})_{w_{\mathcal{P}}} \) is \( w_{\mathcal{P}} \)-dissipative (\( \langle w_{\mathcal{P}}, r_- \rangle = -1 \)).

For \( \mathcal{P} = \{ B \} \) the network is not strongly \( \mathcal{P} \)-endotactic, but \( \mathcal{R}(\mathcal{P}) = \emptyset \).

**Definition 4.5.** A non-empty subset \( \mathcal{P} \subseteq S \) is called a siphon if every reaction \( r \in \mathcal{R} \) with at least one output from \( \mathcal{P} \) also has some input species from \( \mathcal{P} \).

Furthermore, we say that a CRN \((S, C, \mathcal{R})\) with no siphons \( \mathcal{P} \subseteq S \) is asiphonic.

**Remark 4.6.** Def. 4.5 comes from the theory of Petri Nets [26], where it is used to characterize systems that can recover from the extinction of any of their components. This definition is equivalent to the one of exhaustive networks presented in [20].

**Example 4.7.** Consider the CRN
\[ A \rightarrow 2A \rightarrow A \]
It is easy to see that this network is strongly endotactic but has a siphon. This possibly implies issues with the irreducibility of the process \( X_v^w \) (seen as a Markov chain): When \( X_v^w = 2/v \) there is a nonvanishing probability that the next jump will occur in direction \( c^w_2 = -2 \), resulting in the invariant state \( X_v^w = 0 \).

**Example D** (continued). Network (4.1) is asiphonic: The reaction \( \emptyset \rightarrow A + 2B \) has no input from either \( \mathcal{P} = \{ A \}, \{ B \} \), preventing such spaces from being siphons. Network (4.2), on the other hand, has a siphon \( \mathcal{P} = \{ A \} \): All reactions have \( A \) as an input.

We make the following assumption on the topological structure of CRNs. We call \((S, C, \mathcal{R})\) an Asiphonic Strongly Endotactic (ASE) network if it satisfies

**Assumption A.2** ([1] Ass. A.2). The CRN \((S, C, \mathcal{R})\) has the properties:

(a) It is strongly endotactic, as in Def. 4.3
(b) It is asiphonic, i.e., it has no siphon \( \mathcal{P} \subseteq S \).

**Example 4.8.** It is easy to verify that the network
\[ \emptyset \Rightarrow A \rightarrow B \rightarrow C \rightarrow A \]
is ASE: The asiphonic property is verified by the subnetwork \( \emptyset \Rightarrow A \rightarrow B \rightarrow C \), while the fact that \((S, C, \mathcal{R})\) has a single strongly connected component directly implies that the network is strongly endotactic [17].

By Remark 4.6, ASE networks naturally satisfy Assumption A.1(b). This class of networks automatically satisfies Assumption A.1(a) as well.

This is formulated in our main result:
Theorem 4.9 (Existence of a Lyapunov function, [11 Proposition 1.12]). Let

\[ U(x) := d + 1 + \sum_{i=1}^{d} x_i (\log x_i - 1) : \mathbb{R}_+^d \to \mathbb{R}_{\geq 1}. \]  

(4.3)

If the network is ASE, then for the generator \( L_v \) of (2.11) there exists a constant \( b < \infty \) such that for all \( \varrho > 0 \) one can find a \( v^* \) such that for all \( x \) with \( \|x\|_1 < \varrho \), we have for all \( v > v^* \) when \( x \in (v^{-1} \mathbb{N}_0)^d \):

\[ (L_v U_v)(x) \leq e^{bv}. \]  

(4.4)

In other words, for ASE CRNs, the operator \( L_v \) satisfies Assumption A.1 (a) with \( U(x) \) of the form (4.3). Note that \( U(x) \geq 1 \) for all \( x \).

In this paper, we provide an alternative, constructive proof of the above result. To do so, we use a reparametrization of the phase space \( \mathbb{R}_+^d \) that was introduced in [1,17] allowing to treat large-\( \|x\|_1 \) asymptotics of our problem in a particularly natural way. To introduce such a parametrization, we define toric rays, using throughout \( w \in \mathbb{R}^n \), \( z \in (\mathbb{R}_+^n)^o \) and \( \vartheta \in \mathbb{R} > 1 \) and the operators

\[ \log(z) := (\log z_1, \ldots, \log z_n) \in \mathbb{R}^n, \]
\[ z^w := (z_1^w, \ldots, z_n^w) \in (\mathbb{R}_+^n)^o, \]
\[ \vartheta^w := (\vartheta^w_1, \ldots, \vartheta^w_n) \in (\mathbb{R}_+^n)^o. \]

Remark 4.11. The parametrization (4.5) does not cover the point \( z = (1, \ldots, 1) \), but it is irrelevant for our asymptotic analysis.

We next discuss why this reparametrization and the associated Lyapunov function \( U(x) \) of (4.3) are useful. Note that along a \( w \)-toric ray

\[ \nabla U(\vartheta^w) = \log(\vartheta^w) = (\log \vartheta) w, \]  

(4.6)
Fig. 4: Vector field of (2.6) with \( k_1 = k_2 = k_3 = 1 \) under reparametrization of the phase space as \( (\mathbb{R}^d)_o \to \mathbb{R}_{d-1} \times \mathbb{R}^d \setminus \{1\} \) as in (4.5). Note that the tangent bundle of the manifold has not been reparametrized. The red vectors represent the reactions of the network (2.5), and the complex polytope is displayed in light blue. The normals to the edges of this polytope separate the space radially into dominance regions, where the direction of the vector field is asymptotically constant and corresponds to the direction of the dominant reaction.

while the derivative of the ODE (2.3) at a point on such a ray is

\[
\frac{dx}{dt}\bigg|_{x=\vartheta^w} = \sum_{r \in \mathcal{R}} \lambda_r(x)e^r\bigg|_{x=\vartheta^w} = \sum_{r \in \mathcal{R}} k_r(\vartheta^w) e^w c^r = \sum_{r \in \mathcal{R}} k_r(\vartheta^w, c^r) e^r. \tag{4.7}
\]

Thus, at \( x = \vartheta^w \) the time derivative of \( U(x(t)) \) for the solution \( x(t) \) of (2.3) is

\[
\frac{dU(x(t))}{dt}\bigg|_{x=\vartheta^w} = (\nabla U(x), \frac{dx}{dt})\bigg|_{x=\vartheta^w} = (\log \vartheta) \sum_{r \in \mathcal{R}} k_r(\vartheta^w, c^r) \vartheta^{\langle w, c^r \rangle}. \tag{4.8}
\]

One can see that the choice of \( U \) is natural because of (4.8).

For fixed \( w \) and \( \vartheta \gg 1 \) the sum on the rhs of (4.8) is dominated by the set \( \mathcal{R}_w \) of those reactions \( r \) which maximize \( \langle w, c^r \rangle \). As is seen in Fig. 4, far away from the origin the vector field is divided into cells with the flow lines parallel to each other. There are, in this figure, 1-dimensional cells (the isolated lines) and 2-dimensional cells (the 3 regions in the “Mercedes” star). Each 2-dimensional cell corresponds to a set of \( w \in S^{d-1} \) for which one fixed reaction \( r \) is dominating. Furthermore, the direction of the vector field in that region is given by the jump

\(^1\) It can happen that several reactions maximize the scalar product. This will be discussed later.
Fig. 5: The negativity of (4.8) uniformly on $w \in S^{d-1}$ can be visualized as the condition for a large enough radius $\varrho > 0$, the $d$-ball $B_\varrho(0)$ is absorbs the vector field of (4.3) in the new parametrization. As an example, we show that this condition is satisfied by the vector field of (2.6) with $k_1 = k_2 = k_3 = 1$ for $\varrho = 1.9 \times 10^9$. The complex polytope is also plotted, and different dominance regions are separated by the dashed lines.

vector $c^r$ of that reaction. This heuristics also explains our Def. 4.3. In strongly endotactic CRNs, where at least one such reaction contributes negatively to this sum by having $\langle w, c^r \rangle < 0$, and no other reaction $r$ in $\mathcal{R}_w$ contributes positively to it, the LHS of (4.8) will also be negative for all large enough $\vartheta$.

In [17], this geometry was manifestly observed by the authors. The difficulty is to show that the heuristic ideas apply uniformly in $w$. As can be seen from Fig. 4, the uniformity seems obvious in the interior of the 2-dimensional regions, while there are deviations from parallelity near the boundaries of these regions. The question is then whether these curved parts of the vector field point in the right direction or not. We will show that this is indeed the case (as shown in Fig. 5), by giving a constructive proof. This hopefully clarifies what is really going on in the logarithmic representation of the chemical reaction.

**Remark 4.12.** The logarithmic picture does not only apply in the regions where $w_i$ is positive, but also in the opposite case. This corresponds to approaching, as $\vartheta \to \infty$, a boundary of vanishing concentration (in the variable $x_i$). In those directions, the negativity of (4.8) establishes a (polynomial) lower bound on the rate of escape of the ODE solution from the boundary within compact sets [1] Lemma 2.4] provided that the solution does not blow up in finite time. The LDP then implies that the same estimate holds for $X_{t,v}$ starting at the boundary up to an exponentially decaying probability in $v$. 
4.1 Proof of the main theorem (Theorem 4.9)

Following the intuition developed in the previous section the proof is essentially a sequence of asymptotic estimates. They are obtained by covering phase space by open sets which allow to distinguish the different cells and their (carefully) chosen neighborhoods. There is a close relationship between our visualization of the problem and the notion of spherical image of polytopes as developed by Alexandrov in [3, §1.5]. This is a partition of the sphere generated by the set of vectors orthogonal to the polytope, forming cones of dimension \(d - j\) on the \(j\)-dimensional faces of the polytope. If \(W\) is the complex polytope of the network \((S, C, R)\), we denote by \(\tilde{W}_j\) the collection of all its \(j\)-dimensional closed faces. For any \(j < d\), the elements of \(\tilde{W}_j\) are indexed by the set \(I_j\) and denoted by \(\tilde{W}_{j,i}\), for \(i \in I_j\), so that \(\tilde{W}_j = \bigcup_{i \in I_j} \tilde{W}_{j,i}\). We also use the notation \(\partial \tilde{W}_{j,i}\) for the collection of \((j-1)\)-dimensional faces of \(\tilde{W}_{j,i}\), if any, constituting the boundary of \(\tilde{W}_{j,i}\), and set \(I^* := \{(j,i) : j \in (0, \ldots, d-1), i \in I_j\}\).

Throughout, for each \(j\)-dimensional face \(\tilde{W}_{j,i}\) we denote by \(N(\tilde{W}_{j,i})\) the set of normals to the \((d-1)\)-dimensional faces \(W_{d-1,i}\) with \(\tilde{W}_{j,i} \subseteq W_{d-1,i}\) and define the dual \(\tilde{W}_{j,i}^*\) as the \((d-j-1)\)-dimensional intersection \(\tilde{W}_{j,i}^* := \text{Co}(N(\tilde{W}_{j,i})) \cap S^{d-1}\), (4.9)

where \(\text{Co}(A)\) denotes the open conic hull of \(A\). This is precisely the set of \(d\)-dimensional unit normal vectors exposing the facet \(\tilde{W}_{j,i}\). For any convex polytope \(W\), the collection \(\{\tilde{W}_{j,i}^*\}\) forms a unique partition \(W^*\) of \(S^{d-1}\) called the spherical image of \(W\) (see [3, §1.5]). To summarize, we have

\[
W^* := \{\tilde{W}_{j,i}^*\}_{j \in \{0, \ldots, d-1\}}, \quad \text{with} \quad W_{j,i}^* := \{\tilde{W}_{j,i}^*\}_{i \in I_j}.
\]

**Remark 4.13.** The spherical polyhedral complex \(W^*\), used for the study of the asymptotic behavior of polynomials, is well known in the literature under different names. For instance, in tropical calculus it is referred to as the Bieri-Groves complex [7] (or as Bergman fan [6] for the cone over such a spherical complex), while in algebraic geometry this object arises from the intersection of the so-called normal fan [23,25] with the unit sphere.

Using the following parameters we next cover \(S^{d-1}\) by suitable neighborhoods of the elements of \(W^*\).

**Definition 4.14.** We set \(c_* := \max_{r, r^- \in \mathbb{R}} \{\|c^r - c^{r^-}\|_2, \|c^r\|_2\}\) and define, for each \(j \in (0, \ldots, d-1)\),

\[
\begin{align*}
\delta_j(\theta) & := C_{2j}/\log \theta \\
\varepsilon_j(\theta) & := C_{2j+1}/\log \theta \\
\end{align*}
\]

with \(C_{j+1} = K_0 e^{2c_*} c_j\), (4.10)

for some \(K_0 \geq 1\) that is specified in the sequel (see (4.41)).
Fig. 6: Covering of the positive orthant of $S^2$ by sets $\{(W^\ast_j,\iota)_{\in\mathcal{J}} : j \in (0,1,2), \iota \in \mathcal{I}_j\}$ for the network in Example 4.8, whose complex polytope $W$ is drawn, rescaled, in grey. The only element of $W^\ast_2$ in this orthant is the vertex corresponding to the equilateral face of $W$, identified by the vector $n = (1,1,1)/\sqrt{3} \in S^2$ drawn in red in the figure. The $\delta_2$ neighborhood of this point, $(W^\ast_2,0)_{\delta_2}$, is circled in red. The sets $\{(W^\ast_1,\iota)_{\in\mathcal{J}} : j \in (0,1,2), \iota \in \mathcal{I}_j\}$, containing the part of $W^\ast_1$ that has not been covered by $(W^\ast_2,\iota)_{\in\mathcal{J}}$, are also shown in red. The sets defined by the complement of this partial covering, one for each vertex of $W$, are finally contained in $\{(W^\ast_0,\iota)_{\in\mathcal{J}} : j \in (0,1,2)\}$, not shown in the picture.

For $A \subseteq S^{d-1}$ let $A^\delta := \{w \in S^{d-1} : \inf_{v \in A} \|v - w\|_2 < \delta\}$ and for the positive parameters of Def. 4.10 we define $(W^\ast_j,\iota)^{\epsilon_j,\delta_j} := (W^\ast_j \setminus (\partial W^\ast_j)^{\epsilon_j})^{\delta_j}$ for $j < d - 1$ and $(W^\ast_d,\iota)^{\epsilon_d,\delta_d} := (W^\ast_d)^{\delta_d}$ when $j = d - 1$. This induces the covering

$$S^{d-1} = \bigcup_{j=0}^{d-1} \bigcup_{\iota \in \mathcal{I}_j} (W^\ast_j,\iota)^{\epsilon_j,\delta_j},$$

(4.11)

where having $0 < \delta_j < \epsilon_j$ guarantees that for $j < d - 1$, each open set $(W^\ast_j,\iota)^{\epsilon_j,\delta_j}$ does not intersect the boundary of $W^\ast_j$, see Fig. 6. Specifically, through our choice of the $\vartheta$-dependent $(\epsilon_j,\delta_j)$ of Def. 4.14 we cover $S^{d-1}$ by neighborhoods that approach, asymptotically in $\vartheta$, the faces of $W^\ast$.

For any subset of non-extinct species $P \subseteq \mathcal{S}$, the partitions introduced above naturally generalize to the $d_P$-dimensional complex polytope $W(P)$ of the network $(\mathcal{S}, \mathcal{C}, \mathcal{R}(P))$. In particular, we write $W(P) = \{W(P)_{j,\iota} : (j,\iota) \in \mathcal{I}(P)^+\}$, where $\mathcal{I}(P)^+ := \{(j,\iota) : j \in (0,\ldots,d_P - 1), \iota \in \mathcal{I}(P)_j\}$ and $\mathcal{I}(P)_j$ indexes the $j$-dimensional faces of $W(P)$. Moreover, we denote by $W(P)^* = \{W(P)_{j,\iota}^*\}$ the spherical image of $W(P)$ on $S^{d_P-1}$ and by $\{(W(P)_{j,\iota})^{\epsilon_j,\delta_j}\}$ the corresponding covering of $S^{d_P-1}$.

We proceed to prove Theorem 4.9 by showing for each face $W_{j,\iota}$ the (somewhat stronger) bound...
Proposition 4.15. For any $j, \iota$ and sufficiently large $\varrho_0 \geq 3 \delta$, one has for all $w \in (W_{j,\iota}^*)^0 \setminus \partial \mathcal{D}$, $\varrho > \varrho_0$, $v > v^*(\varrho) := e^\varrho$ and $x = \vartheta^w \in (v^{-1}N(0))^w$ with $\varrho_0 < \|x\|_1 < \varrho$, that

$$\mathcal{L}_v U^v(\vartheta^w) = v \sum_{r \in R} A_{r,v}(\vartheta^w) \left( U^v(\vartheta^w + v^{-1}e^c) - U^v(\vartheta^w) \right) < 0. \quad (4.12)$$

Definition 4.16. Throughout, we refer to the relations set in Proposition 4.15 between the quantities $\varrho_0, \varrho, w, x, v^*$ and $v$ as the standard conditions. These choices will continue to hold throughout the section, where in particular $\log \vartheta \geq 1$ (since $d \vartheta \geq \|x\|_1 > 3 \delta$).

Remark 4.17. Proving Proposition 4.15 results with (4.4). Indeed, fixing $\varrho_0$ large enough (that accommodates all $j, \iota$ pairs), for $v > v^*(\varrho)$ and $\varrho_0 < \|x\|_1 < \varrho$ the inequality (4.4) is satisfied by (4.12), while for $\|x\|_1 \leq \varrho_0$ we get (4.4) from

$$\mathcal{L}_v U^v(x) = v \sum_{r \in R} A_{r,v}(x) \left( U^v(x + v^{-1}e^c) - U^v(x) \right) \leq m \sup_{r \in R, \|x\|_1 \leq \varrho_0} \left\{ \lambda_r(x) \right\} \sup_{\|x\|_1 \leq \varrho_0, \|e^c\|_1} \left\{ vU(x)^v \right\} \leq e^{b(\varrho_0)^v}.$$

Remark 4.18. Def. 4.10 can be understood heuristically by inspection of (4.8). For every face $W_{j,\iota}$ through our choice of $\{ \varepsilon_j, \delta_j \}$ we are ensuring that the reaction rate of dominant reactions is larger than any other by at least a factor of $e^{K_j C_2 \delta_j}$ for a constant $K_j > 1$. This choice also guarantees that the scalar product contribution, i.e., $\langle w, e^c \rangle \log \vartheta$, of at least one among such reactions is negative and bounded away from zero, while all the others are at most $C_2$, (from the definition of strongly endotactic CRN). Choosing $C_{2j+1}$ large enough wrt $C_{2j}$ establishes the desired bound (4.12).

4.1.1 Face-dependent estimates

To prove Proposition 4.15 consider now a fixed face $\mathcal{F} = W_{j,\iota}$ with spherical image $\mathcal{F}^* = W_{j,\iota}^*$. For $w \in \mathcal{F}$ we define a partition of $R = R_+ \cup R_0 \cup R_-$ (which depends on $\iota$ and $j$):

- $R_-$ are those reactions with $\epsilon_1^w \in \mathcal{F}$ that are $w$-dissipative,
- $R_0$ are those reactions with $\epsilon_0^w \in \mathcal{F}$ that are $w$-null,
- $R_+$ are those reactions for which $\epsilon_n^w \notin \mathcal{F}$.

The case $\epsilon_n^w \in \mathcal{F}$ and $\langle w, e^c \rangle > 0$ is excluded because the networks are assumed to be strongly endotactic. This property also ensures that the set $R_-$ is nonempty for all $w$. This partition of $R$ naturally generalizes to a partition of $R(\mathcal{P})$ generated by any face of the polytope $W(\mathcal{P})$ and the corresponding dual from $W(\mathcal{P})^*$.

Remark 4.19. Consider the set $R_\mathcal{F} = \{ r \in \mathcal{R} : c_n^w \in \mathcal{F} \}$. Note that $r \in R_\mathcal{F}$ maximizes $\langle w, c_n^w \rangle$ for all $w \in \mathcal{F}^*$. That is, $\langle w, c_n^w - c_m^w \rangle < 0$ whenever $r \notin R_\mathcal{F}$. In particular, $R_w = R_w(\mathcal{S}) = R_\mathcal{F}$ for any such $w$. Further, by continuity $(n, c_n^w - c_m^w) \leq 0$ for all $n \in N(\mathcal{F})$, with equality for a $r \notin R_\mathcal{F}$ iff $c_n^w \in W_{d-1,\iota}$ and $\mathcal{F} \subset \partial W_{d-1,\iota}$ for some face $W_{d-1,\iota}$ to which $n$ is normal.
Remark 4.20. By Remark 4.19, the preceding decomposition does not depend on \( w \in \mathcal{F} \) (i.e., \( \langle w, c_r \rangle < 0 \) for any \( r \in \mathcal{R}_- \) and \( w \in \mathcal{F}^* \)). Indeed, if \( \langle w_0, c'_r \rangle = 0 \) and \( \langle w_1, c'_r \rangle < 0 \) for some \( w_0, w_1 \in \mathcal{F}^* \) and \( r \in \mathcal{R}_F \), then since \( \mathcal{F}^* \) is open \( w_2 := w_0 - \eta w_1 \in \mathcal{F}^* \) for some \( \eta > 0 \) small enough, with \( \langle w_2, c'_r \rangle > 0 \) and \( r \in \mathcal{R}_{w_2} \) in contradiction with our assumption that the network is strongly endotactic.

Defining
\[
Q_{r,v}(x) := U(x) \left[ U^v(x + v^{-1} c'_r) / U^v(x) - 1 \right],
\]
we will obtain (4.12) by showing that under our standard conditions, for any \( r_- \in \mathcal{R}_- \), and all \( w \in (\mathcal{F}^*)^{\mathcal{I}_W} \), we have \( Q_{r_-,(v)}(x) < 0 \) and
\[
\sum_{r \in \mathcal{R}_+ \cup \mathcal{R}_0} A_{r_-,(v)}(\vartheta^w_r) Q_{r,v}(\vartheta^w_r) < -Q_{r_-,(v)}(\vartheta^w_r).
\]

As the map (4.5) has \( (\mathbb{R}^d)^n \) as domain, in order to establish Theorem 4.9 on \( \partial \mathbb{R}^d \), the program summarized above has to be carried out on each \( \mathcal{P} \subseteq \mathcal{S} \) separately.

### 4.1.2 Bounding terms

We devote this section to bounds on the summands of (4.12) depending on their classification into \( \mathcal{R}(\mathcal{P})_+ \), \( \mathcal{R}(\mathcal{P})_0 \) or \( \mathcal{R}(\mathcal{P})_- \). We do this in two phases. First, in Corollary 4.22, we show that under our standard conditions there exists \( K_1 < \infty \) such that for all \( r \in \mathcal{R}(\mathcal{P})_-(w) \), \( w_\mathcal{P} \in (\mathcal{W}(\mathcal{P})_{j,i})^{\mathcal{I}_W} \),
\[
\frac{A_{r,(v)}(\vartheta^w_r)}{A_{r_-,(v)}(\vartheta^w_{r_-})} \leq K_1 \vartheta^{(w_\mathcal{P} c'_r - c'_{r_-})}.
\]

Then, in Lemmas 4.24–4.25, we bound the terms \( Q_{r,v}(x) \) from above. For \( r \in \mathcal{R}(\mathcal{P})_+ \) or \( \mathcal{R}(\mathcal{P})_0 \) this limits the possibly positive contribution of such terms, while ensuring a negative enough contribution for \( r_- \in \mathcal{R}(\mathcal{P})_- \). We call those terms the Lyapunov terms, as opposed to the monomial terms in (4.15).

We now proceed with the first part of our program. Fixing \( \mathcal{P} \subseteq \mathcal{S} \) and \( (j,i) \in \mathcal{I}(\mathcal{P})^* \), consider \( w = w_{j,i} \in (\mathcal{W}(\mathcal{P})_{j,i})^{\mathcal{I}_W} \).

The estimate from [11] (3.18) presented in Lemma 4.21 is crucial for the understanding of the dynamics near vanishing densities when one establishes 4.15. We illustrate the ideas in the proof of this result for the 2-dimensional case of Fig. 2. Given any vector \( w \) of length 1, we say that it exposes the reaction(s) originating in the 0-dimensional face of \( \mathcal{W} \) to which \( w \) is dual. In the example, writing \( w = (\cos \phi, \sin \phi) \), we see that \( w \) exposes
\[
(1, 2), \text{ if } \phi \in (-\pi/6, \pi/4),
(0, 3), \text{ if } \phi \in (\pi/4, \pi),
(0, 0), \text{ if } \phi \in (\pi, 11\pi/6).
\]
Here, \((1, 2)\) is the origin of the reaction \(A + 2B \to 3B\), and similarly for the others. For our example, the 3 cases have, respectively, 0, 1, or 2 points on an axis. Consider one of the arcs above (or its exposed reaction). We call such an arc non-critical if its closure contains a direction which coincides with a negative axis, and otherwise, critical. So \((0, 3)\) is non-critical, as it contains the negative \(A\) axis; \((0, 0)\) is non-critical, containing the negative \(A\) and \(B\) axis; \((1, 2)\) is critical.

The issue is now that the discrete reaction rates (2.12) may differ significantly from the continuous ones (2.4). For the example, we need to compare (setting \(WLOG\) \(k_1 = k_2 = k_3 = 1\))

\[
\begin{align*}
(1, 2) : & \quad x_A x_B^2, \quad \text{and} \quad v^{-3} \left( \frac{v x_A}{1} \right) \left( \frac{v x_B}{2} \right) 1! 2!, \\
(0, 3) : & \quad x_B^3, \quad \text{and} \quad v^{-3} \left( \frac{v x_B}{3} \right) 3!, \\
(0, 0) : & \quad 1, \quad \text{and} \quad 1,
\end{align*}
\]

depending on the continuous model, respectively the discrete one in volume \(v\).

We start with the non-critical case \((0, 0)\). Here, the rates are obviously equal. In the case \((0, 3)\), which is also non-critical, we see that the rates do not depend on \(x_A\): \((c^w_{in})_A = 0\). In the corresponding arc, \(w_B \geq 0\). Hence, \(x_B \geq 1\) and

\[
\frac{v^{-3} (v x_B) 3!}{x_B^3} = 1 - O \left( \frac{1}{v x_B} \right),
\]

when \(v\) is large.

The critical case \((1, 2)\) is more interesting: If the angle \(\phi\) is positive, then both components of \(\vartheta^w\) diverge to \(\infty\) as \(\vartheta \to \infty\), and therefore

\[
\frac{A_{\vartheta, v}(x)}{\lambda_\vartheta(x)} = \frac{v^{-3} (v x_A) (v x_B) 1! 2!}{x_A x_B^2} = 1 - O \left( \frac{1}{v x_B} \right), \quad (4.16)
\]

However, when \(\phi \in [-\pi/6, 0]\), a more careful estimate is needed. We reparameterize \(v\) and \(x\) as follows: We fix \(\vartheta\), a distance from the origin, and require, as in our standard conditions,

\[
v \geq e^{\vartheta}, \quad (4.17)
\]

and

\[
(x_A, x_B) = \vartheta^w, \quad \text{with} \quad \vartheta \geq \|\vartheta^w\|_1 \geq \vartheta^{1/2}, \quad (4.18)
\]

where in the last inequality we have used that for our choice of \(\phi\), we have \(w_A > 1/2\). In this case, the orbit of \(\vartheta^w\) approaches the \(\{B = 0\}\) axis as \(\vartheta\) grows, but the distance from the \(\{B = 0\}\) axis is bounded below by \(\vartheta^{-\cos(\pi/6)} = \vartheta^{-1/2}\). Therefore, we again find that

\[
v x_B \geq e^{\vartheta} \cdot (2\vartheta^2)^{-1/2},
\]
which again grows beyond bounds as $\varrho \to \infty$. Therefore, (4.16) holds again, with a r.h.s. $1 - O(\varrho e^{-\varrho})$. We will use a slightly stronger variant: Since $e^{\varrho} \varrho^{-1/2}$ diverges and rate terms behave polynomially in $\varrho$, we find for any $\mu \in (0, 1)$

$$
\lim_{\varrho \to \infty} \varrho^w v^\mu = \infty ,
$$

which we will use in the form

$$
\lim_{\varrho \to \infty} \mu \log v + w_B \log \varrho = \infty ,
$$

(4.19)

with our choice of (4.17) and (4.18).

Having motivated the example in all detail, the extension to an arbitrary chemical network is straightforward, but we need to generalize properly the critical case. We do so in the following lemma, where we establish another bound similar to (4.19) for later use.

**Lemma 4.21.** Consider a face $F \in W(P)$ and the corresponding decomposition of $R(P)$. Then for any $\mu \in (0, 1)$, $M < \infty$, there exists $\varrho_0(\mu, M, C_2)$, such that under our standard conditions, for $w \in (F^*)^{c, \beta}$ and $x = \varrho^w$,

$$
\mu \log v - w_i \log \varrho > M .
$$

(4.20)

**Proof.** We fix $\beta := 1/\sqrt{d_P}$ and $w \in (F^*)^{c, \beta}$, and we prove the desired results in the following cases:

- If $\max \{ w_i \} \geq \mu \beta/(2c_\ast) =: \eta$, then we have $d\varrho \geq \| x \|_1 > \varrho_0$, $\log v > \| x \|_1\geq \varrho^{-\eta}$ and it follows that

$$
\mu \log v - w_i \log \varrho > \inf_{\varrho > \varrho_0/d} \{ h(\varrho) \} > M ,
$$

for $h(\varrho) := \mu \varrho^{\eta} - \log \varrho$ and $\varrho_0 = \varrho_0(\mu, M)$ large enough, concluding the proof in this regime.

- Alternatively, $\max \{ w_i \} < \eta < \beta$ requires $w_{l'} \leq -\beta$ for some $l' \in P$. Consequently, as $w_{l' \in N}$, we have that $v \geq \varrho^\beta$. With $\eta \leq \eta c_\ast = \mu \beta/2$, we obtain

$$
\mu \log v - w_i \log \varrho \geq (\mu \beta - \eta \log \varrho > M ,
$$

provided $\varrho(\mu, M)$ is large enough, which proves (4.20). To prove (4.21), we fix some $r \in R(P)_- \cup R(P)_0$ with $(e_{in}^r)_i > 0$ and show that (4.21) holds. Recall from Assumption $A.3$ (b) that $c_{\ast 0}^r = 0$ for some $r \in R$. Hence, we have from Remark 4.19 that $0 \leq \langle w', e_{in}^r \rangle$ for all $w' \in F^*$. Having $w' \in F^*$ with $\| w - w' \|^2_2 < \delta$ yields

$$
0 \leq \langle w', e_{in}^r \rangle \leq \langle w, e_{in}^r \rangle + \delta c_\ast < w_i (e_{in}^r)_i + (\eta + \delta)c_\ast ,
$$

which in turn implies that $w_i > -(\eta + \delta)c_\ast$. Combining this with $\delta = C_2/\log \varrho$ (see Def. 4.14), we finally have

$$
\mu \log v + w_i \log \varrho > (\mu \beta - \eta c_\ast) \log \varrho - c_\ast C_2 \geq M
$$

provided that $\varrho_0 > \exp(2(M + c_\ast C_2))/(\mu \beta))$. $\square$
We show that (4.15) is a direct consequence of Lemma 4.21.

**Corollary 4.22.** Under our standard conditions, (4.15) holds for some $K_1$ finite, any $(j, i) \in \mathcal{I}(P)^* \cap \mathbb{R}(P)$, $r \in \mathcal{R}(P)$. 

**Proof.** Letting $\xi(k) := k!k^{-k}$ for $k \in \mathbb{N}$ and $\xi(0) = 1$, we set 

$$x_r := \prod_{i=1}^{d} \xi((c_i^{r})_i) > 0 .$$

Comparing (2.12) and (2.4) we have $A_{r,v}(x) \leq \lambda_v(x)$ for any $x \in (v^{-1}N_0)^{d\rho}$, $v \geq 1$. Further, the ratio $A_{r,v}(x)/\lambda_{r,v}(x)$ is non-decreasing in each $v x_i$ and equals $x_{r,v}$ when $v x = c_i^{r,v}$. Since by (4.21) with $M = \log c_r$ and $\mu = 1$ we have $v x_i \geq (c_i^{r,v})_i$ for any $v > v^*(y_0)$, $r_-, v \in (\mathbb{R}^*)^{-\delta}$, $i \leq d$, the claim follows by setting $K_i := \max_{r} \{x_r(k_r)\} / \min_{r} \{x_r(k_r)\}$.

We now turn to the second part of this section, dedicated to upper bounds on the Lyapunov terms $Q_{r,v}(x)$. We will first estimate these terms by approximating, in Lemma 4.23 $U(x + v^{-1}c^r)/U(x)$ as an exponential, whose argument is then bounded from above in Lemmas 4.24, 4.25 based on geometric considerations. Note that $U(x + v^{-1}c^r) - U(x)$ is a sum of terms of the form

$$T_i = (x_i + v^{-1}c_i^r) \log(x_i + v^{-1}c_i^r) - (x_i + v^{-1}c_i^r) - x_i \log x_i + x_i .$$

We bound $T_i$ according to 3 cases:

(a) If $i \in \mathcal{P}$ then we know $x_i \geq v^{-1}$ and we bound $v T_i$ by $c_i^r \log x_i + g(r, v, x_i)$.

We show below that $|g(r)|$ is globally bounded.

(b) If $i \in \sup \{c_{i,\text{out}}^r\} \cap \mathcal{P}$ then $v T_i = c_i^r \log(v^{-1}c_i^r) + g(r, v, x_i)$.

(c) In the remaining case $(c_{i,\text{out}}^r)_i = 0$ and hence $T_i = 0$.

In view of the above, we define as in [1]

$$\langle \nabla_{r,v} U \rangle := \begin{cases} \log x_i, & i \in \mathcal{P} \\ \log(v^{-1}c_i^r), & i \in \sup \{c_{i,\text{out}}^r\} \cap \mathcal{P} \\ 0, & \text{otherwise} \end{cases} . \quad (4.23)$$

**Lemma 4.23 (Lemmas 3.4, 3.6).** There exist finite $v_0$ and $\zeta_*$ such that for any $\mathcal{P} \subseteq \mathcal{S}$, $r \in \mathcal{R}(\mathcal{P})$, $v \geq v_0$ and $x \in (v^{-1}N_0)^{d}$ with $\sup \{x\} = \mathcal{P}$ and $x + v^{-1}c^r \in (v^{-1}N_0)^{d}$, one has

$$\frac{U^v(x + v^{-1}c^r)}{U^v(x)} = \exp \left\{ \frac{h_{r,v}(x) + \zeta_*(v, x)}{U(x)} \right\} , \quad (4.24)$$

for $h_{r,v}(x) := \langle \nabla_{r,v} U(x), c^r \rangle$ and a function $\zeta_*(v, x)$ with $|\zeta_*(v, x)| \leq \zeta_*$. 

Proof. Since the number of possible \( P \) and \( r \) is finite, it suffices to prove the claim for fixed \( P \) and \( r \in R(P) \). To this end, we conveniently write the rhs of (4.24) as

\[
\frac{U^v(x + v^{-1}c^v)}{U^v(x)} = \left( 1 + \frac{f}{v} \right)^v = \exp \left[ \frac{fU(x) - vU(x)R(f/v)}{U(x)} \right],
\]

where \( f := v[U(x + v^{-1}c^v) - U(x)]/U(x) \) and \( R(y) := y - \log(1 + y) \). We then define

\[
\zeta_r(v, x) := g_r(v, x) - vU(x)R(f/v)
\]

where \( g_r(v, x) := fU(x) - h_{r,v}(x) \), and proceed to bound the terms on the rhs of (4.25) separately. To this end, with \( \psi(b, c) := (b + c) \log(1 + c/b) \), we have when \( \operatorname{supp}\{x\} \subseteq P \) that

\[
g_r(v, x) = \sum_{j \in P} \psi(vx_j; c^r_j) - \langle c^r, \mathbb{1} \rangle.
\]

Since \( \psi(b, c) \) decreases in \( b \geq \max(1, -c) \), it is easy to verify that \( |g_r(v, x)| \) is uniformly bounded over \( vx \) as in the statement of the lemma.

With \( R(y) \leq 2y^2 \) when \( y \geq -1/2 \), we globally bound the remainder in (4.25) upon showing that for some \( v_0 \) finite and all \( v \geq v_0 \)

\[
vU(x) \left( \frac{2f}{v} \right)^2 \leq \frac{8h_{r,v}(x)^2}{vU(x)} + \frac{8g_r(v, x)^2}{vU(x)}, \quad (4.26)
\]

is uniformly bounded above by \( v_0 \). Since \( U(x) \geq 1 \), the rightmost term is obviously \( O(1/v) \). Further, to globally bound the first term on the rhs of (4.26), it suffices to control

\[
\sup_{v \geq 1} \left\{ \frac{|\log y|^2}{v[y(\log y - 1) + 2]} \right\}.
\]

For \( y \in [v^{-1}, v] \) this quantity is at most \((\log v)^2/v \to 0 \) as \( v \to \infty \), whereas for \( y \geq v \geq e^2 \) it is at most \( 2 \log y/\log y \leq 2 \log v/v^2 \to 0 \) as \( v \to \infty \). Hence, some finite \( v_0 \) will bound the lhs of (4.26) uniformly in \( v \geq v_0 \) and \( x \) as stated.

From Corollary 4.22 and Lemma 4.23, we see that a comparison of \( \langle w, c^v \rangle \) and \( \langle w, c^v_{\infty} - c^v_{-\infty} \rangle \) is needed for bounding summands of (4.14) from above, as was done in (4.8).

Lemma 4.24. For any \( P \subseteq S \), \( (j, \iota) \in \mathcal{I}(P)^* \), there exist \( K_2 \in (0, 1) \) and \( K_2 \in [1, \infty) \), such that if \( c^r \delta_j \leq K_2 \varepsilon_j, \varepsilon_j < 1/2 \), then for all \( w \in (W(P)^*)^{r, \delta_j} \):

(a) \( \langle w, c^r \rangle \leq c^r \) for all \( r \in R(P) \),
(b) \( \langle w, c^r \rangle < c^r \delta_j \) for all \( r \in R(P)_- \cup R(P)_0, \supp c^r \subseteq P \),
(c) \( \langle w, c^r_{\infty} - c^r_{-\infty} \rangle < c^r \delta_j \) for all \( r \in R(P)_- \cup R(P)_0, r_\in R(P)_- \),
(d) \( \langle w, c^r_{\infty} - c^r_{-\infty} \rangle < -K_2 \varepsilon_j \) for all \( r \in R(P)_+, r_\in R(P)_- \),
(e) \( \langle w, c^r \rangle < -K_2 \varepsilon_j \) for all \( r_\in R(P)_- \supp c^r \subseteq P \),
(f) \( \langle w, c^r \rangle \leq -K_2 \langle w, c^r_{\infty} - c^r_{-\infty} \rangle \) for \( r, r_\in R(P)_- \) as in (d).
Proof. Fixing $\mathcal{P} \subset S$, $(j, i) \in \mathcal{I}(\mathcal{P})^*$, we abbreviate throughout $\mathcal{F}^* = \mathcal{W}(\mathcal{P})^*$, $\varepsilon = \varepsilon_j, \delta = \delta_j$ and $z = r^c_{\text{in}} - c^r_{\text{in}}$. Note that part (a) is merely the trivial inequality
\[
\langle w, c' \rangle \leq \|c'\|_2 \leq c_\star.
\]
For any $w \in (\mathcal{F}^*)^{\varepsilon, \delta}$ we have
\[
\|w - w'\|_2 < \delta \quad \text{for some} \quad w' \in (\mathcal{F}^*)^{0, 0} \subset \mathcal{F}^*,
\]
and part (b) similarly follows, as $\langle w', c' \rangle \leq 0$ whenever $r \in \mathcal{R}(\mathcal{P})_+ \cup \mathcal{R}(\mathcal{P})_0$ and $\text{supp} c' \subseteq \mathcal{P}$ (see Def. 4.1 and Remark 4.20). Combining (4.27) with the inequality $\langle w', z \rangle \leq 0$ for any $w' \in \mathcal{F}^*$, $r \in \mathcal{R}(\mathcal{P})$ and $r_- \in \mathcal{R}(\mathcal{P})_-$ (from Remark 4.19), proves (c). Further, $(w', z)$ is negative whenever $r \in \mathcal{R}(\mathcal{P})_+$ and $r_- \in \mathcal{R}(\mathcal{P})_-$, with $\langle w', c' \rangle$ negative if in addition $\text{supp} c' \subseteq \mathcal{P}$. Thus, considering $c_\star \delta \leq K_2 \varepsilon$ and the finite set
\[
\Xi := \{ z : r \in \mathcal{R}(\mathcal{P})_+, r_- \in \mathcal{R}(\mathcal{P})_- \}
\]
parts (d) and (e) follow upon finding $K_2 \in (0, 1)$ such that for $\varepsilon > 0$ and $\xi \in \Xi$,
\[
\inf_{w \in (\mathcal{F}^*)^{0, 0}} \{ |\langle w, \xi \rangle| \} \geq 2K_2 \varepsilon.
\]
Since $\Xi$ is finite, it suffices to establish (4.28) for each fixed $\xi \in \Xi$. Further scaling wlog such $\xi$ to be a unit vector, we can write
\[
|\langle w, \xi \rangle| = \inf_{x \in H^+(\xi)} \|w - x\|_2 := g(w).
\]
Note that the hyperplane $H^+(\xi)$ perpendicular to $\xi \in \Xi$ is disjoint of $\mathcal{F}^*$, or else we would have had $c^r_{\text{in}} \in \mathcal{F}$ for some $r \in \mathcal{R}(\mathcal{P})_+$ or $c^r_{\text{out}} \in \mathcal{F}$ for some $r_- \in \mathcal{R}(\mathcal{P})_+$ for which $\text{supp} c' \subseteq \mathcal{P}$ in contradiction with our partition of $\mathcal{R}(\mathcal{P})$ (see also Def. 4.1). Using this, we first consider the case $j = 0$, where the cap $\mathcal{F}^*$ has a positive $(d_p - 1)$-dimensional surface area. Then, as illustrated in Fig. 7, we have for any $\varepsilon < 1/2$ and $w \in (\mathcal{F}^*)^{0, 0}$, that
\[
g(w) \geq \inf_{x \in \partial \mathcal{F}^*} \{ \sin(\angle(w, x)) \} \geq \sin(\varepsilon) > \varepsilon/2.
\]
Next, if $1 \leq j \leq d_p - 2$, then the unique $(d_p - j)$-dimensional hyperplane $H_{j+1}(\mathcal{F}^*)$ containing $0$ and all of $\mathcal{F}^*$, has a positive dihedral angle
\[
\gamma := \angle \left( H^+(\xi), H_{j+1}(\mathcal{F}^*) \right) \in (0, \pi/2]
\]
with $H^+(\xi)$, see Fig. 8a for an illustration.\(^\dagger\)

As depicted in Fig. 8b, we then bound $g(w)$ by further restricting $x$ to be on $H_{j+1}(\xi)$. At the cost of a constant factor $\sin \gamma$, this reduces the problem to that of
\(^\dagger\) where the angle between hyperplanes $A, B \subset \mathbb{R}^d$ passing through the origin is
\[
\angle(A, B) := \arccos(\max \{ \min \{ |\langle a, b \rangle| : a \in A, \|a\|_2 = 1 \} : b \in B, \|b\|_2 = 1 \}).
Fig. 7: Representation of the geometric construction used in the proof of (4.28) for $j = 0$. The faces of $\mathcal{W}(\mathcal{P})$ adjacent to $\mathcal{F}$ are denoted by dashed black lines, the dual $\mathcal{F}^*$ is drawn in red together with its $\varepsilon$-boundaries and an element $w \in \mathcal{F}^*$ drawn as a solid red arrow. For a certain $\xi$ (solid black vector), we have drawn in green the $(\varepsilon/2)$-neighborhood of the blue $H^1(\xi)$, with a light blue line-segment for the distance between $w$ and $H^1(\xi)$. That distance (a) equals or (b) is greater than $\inf_{x \in \partial \mathcal{F}^*} \{ \sin(\angle(w, x)) \}$ (denoted as a dashed blue line in (b)).

\[ j = 0 \text{ treated above. Indeed, combining (4.29) with } \sin(\gamma) \geq 2\gamma/\pi \text{ we obtain for any } \varepsilon < 1/2 \text{ and } w \in (\mathcal{F}^*)^{\varepsilon,0} \text{ that} \]

\[ g(w) = \sin(\gamma) \inf_{x \in H^1(\xi) \cap H_{j+1}(\mathcal{F}^*)} \| w - x \|_2 \geq \frac{2\gamma}{\pi} \inf_{x \in \partial \mathcal{F}^*} \{ \sin(\angle(w, x)) \} \geq \frac{\gamma\varepsilon}{\pi}. \]  

(4.30)

Last, for $j = d_P - 1$, the same reasoning can be applied by setting $(\mathcal{F}^*)^{\varepsilon,0} = \mathcal{F}^*$. As $H_{j+1}(\mathcal{F}^*) \cap H^1(\xi) = 0$, we obtain $g(w) = \sin(\gamma) \geq 2\gamma/\pi$, verifying (4.28) for $\vartheta_0 = \vartheta_0(K_2, \gamma)$ large enough. In conclusion, we have (4.28) with $K_2 := 1/4$ when $j = 0$ and $K_2 := \gamma/(2\pi)$ when $j > 0$, thanks to (4.29) and (4.30), respectively.

Part (f) asserts that $\langle w, c^* + K_3z \rangle \leq 0$ on $(\mathcal{F}^*)^{\varepsilon,0}$. Since $c^* \delta \leq K_2\varepsilon$, it suffices to show that

\[ \langle w, c^* + K_3z \rangle \leq 0 \quad \forall \ w \in \mathcal{F}^*. \]  

(4.31)

Indeed, as $w \in (\mathcal{F}^*)^{\varepsilon,0}$ is within $\delta$ of some $w' \in \mathcal{F}^*$ for which $\langle w', z \rangle \leq -2K_2\varepsilon$ (c.f. (4.28)), the argument leading to (d) then gives for $K_3 := 1 + 2K_3'$

\[ \langle w, c^* + K_3z \rangle \leq \langle w', c^* + K_3z \rangle + c_4 \delta(1 + K_3^1) \leq (K_3 - K_3')(w', z) + K_2\varepsilon(1 + K_3^1) \leq 2K_2\varepsilon(K_3' - K_3) + K_2\varepsilon(1 + K_3) = 0. \]

Finally, to prove (4.31) it suffices to check that the linear functional on its LHS is non-positive in the finite set of extreme directions $\mathcal{N}(\mathcal{F})$. This results from the fact that $r \in \mathcal{R}(\mathcal{P})_+$ and Def. 4.3 of strongly endotactic CRN: indeed either
Fig. 8: Representation of the geometric construction used in the proof of Lemma 4.24 for \( j \neq 0 \), with the same notations as Fig. 7. The part of \( H_{j+1}(F^*) \) containing \( F^* \) is drawn in red and the dihedral angle \( \gamma \) in dotted blue. Fig. (b) is an inset of Fig. (a), where the light blue distance of \( w \) from \( H^\perp(\xi) \cap H_{j+1}(F^*) \), equals \( \sin \gamma \) times the distance between \( w \) and its projection \( x^* \) onto \( H^\perp(\xi) \).

\[
z_n := \langle n, z \rangle < 0 \text{ (see Remark 4.19)}, \text{ or, if } c_{r_{in}} \text{ is on a } (d_P - 1)\text{-dimensional face of } W(P) \text{ perpendicular to } n, \text{ then } \langle n, z \rangle = 0. \text{ In the latter case, however, by Def. 4.3 and our partition of } R(P) \text{ we have } \langle n, c^r \rangle \leq 0. \text{ Thus, (4.31) holds for any } K_3 \leq \max\{c_{r_{in}}/|z_n| : n \in N(F), z_n \neq 0\}. \]

Utilizing again Lemma 4.21, we next bound the contribution of possibly dominant reactions with \( \text{supp } c_{r_{out}} \not\subseteq P \).

**Lemma 4.25.** Choose \( K_4 < \infty \). Then, there exists \( \varrho_0 \) such that under our standard conditions, for any \( P \subseteq S \), face \( F \in W(P) \) and \( r \in R(P)_- \) with \( \text{supp } c_{r_{out}} \not\subseteq P \), we have

\[
h_{r,v}(\vartheta^w) < -K_4 \quad \text{for all } \quad w \in (F^*)^{c,\delta}.
\]

**Proof.** Fixing \( r \in R(P)_- \) with \( \text{supp } c_{r_{out}} \not\subseteq P \), set \( \varkappa := \sum_{i \notin P} c_{r_{in}} \log c_{r_{in}} \) finite, \( \beta := \sum_{i \in P} c_{r_{in}} \geq 1 \) and \( \mu := 1/\|c^r\|_1 \in (0, 1) \). Then, for any \( w = w_P \in (F^*)^{c,\delta} \),

\[
\varkappa - h_{r,v}(x) = \beta \log v - \langle w, c^r \rangle \log \vartheta \geq \log v - \langle w, c^r \rangle \log \vartheta.
\]

(4.32)

If \( c_{r_{in}} = 0 \) for all \( i \in P \) then \( \langle w, c^r \rangle = 0 \) and we are done. Otherwise, setting \( M = \varkappa + K_4 \), note that if \( c_{r_{in}} < 0 \) then \( c_{r_{in}} \geq 1 \) and (4.21) applies, while (4.20) applies for all \( i \in P \). We thus get from (4.32)

\[
\varkappa - h_{r,v}(x) \geq \sum_{i \in P} |c_{r_{in}}| (\mu \log v - \text{sign}(c_{r_{in}}) w_i \log \vartheta) > M \sum_{i \in P} |c_{r_{in}}| \geq \varkappa + K_4.
\]

We can find \( \varrho_0(K_4) \) large enough to apply for all faces, reactions and species. \( \square \)

We next combine Corollary 4.22, Lemma 4.23 and Lemma 4.24 to control the contribution to (4.14) by the reactions in \( R(P)_+ \cup R(P)_0 \).
Corollary 4.26. Suppose \( C_{2j+1} \geq c_4 C_{2j}/K_2 \) as in Lemma 4.24. Then for some \( K_5 = K_5(K_1, K_3, \zeta_4) \) finite, any \( \mathcal{P} \subseteq \mathcal{S} \), \( (j, i) \in \mathcal{I}(\mathcal{P})^* \) and \( r_- \in \mathcal{R}(\mathcal{P})_- \), under our standard conditions

\[
\sum_{r \in \mathcal{R}(\mathcal{P})_+ \cup \mathcal{R}(\mathcal{P})_0} \frac{A_{r,v}(x)}{A_{r-,v}(x)} Q_{r,v}(x) < m K_5 e^{2c_4 C_{2j}}. \tag{4.33}
\]

Proof. From (4.23) we see that a component outside \( \mathcal{P} \) with \( c_{\text{out}}^r \) contributes negatively to \( h_{r,v}(x) \) if \( v \geq \max(v_0, c_4 e^{2c_4}) \). In other words, for \( g_0 \) large enough, restricting \( c_{\text{out}}^r \) to \( \mathcal{P} \) can only increase the value of \( Q_{r,v}(\cdot) \). Therefore, if \( \text{supp}(c_{\text{out}}^r) \not\subseteq \mathcal{P} \), we consider instead (4.33) for \( c_{\text{out}}^r \) restricted to \( \mathcal{P} \). Hence, wlog we set \( \mathcal{P} = \mathcal{S} \) and having then \( h_{r,v}(x) = \langle w, c^r \rangle \log \theta \), we can write \( h_{r,v}(x) + \zeta_4(v, x) \leq 2 \max(\langle w, c^r \rangle \log \theta, \zeta_4) =: f_r(x, \zeta_4) \). Furthermore, since \( U(\cdot) \) has compact level sets, for large enough \( g_0 \) we have \( U(x) \geq 4K_3 \). Consequently, since \( e^{-y} - 1 \leq \max(y, 0) e^y \) combining (4.13) and (4.24) we bound Lyapunov terms from above by

\[
Q_{r,v}(x) = U(x) \left( \exp \left[ \frac{h_{r,v}(x) + \zeta_4(v, x)}{U(x)} \right] - 1 \right) \leq f_r(x, \zeta_4) e^{f_r(x, \zeta_4)/4K_3} < 4K_3 e^{f_r(x, \zeta_4)/2K_3}. \tag{4.34}
\]

We proceed to obtain (4.33) by considering reactions in \( \mathcal{R}_+ \) and \( \mathcal{R}_0 \) separately. For \( r \in \mathcal{R}_+ \), by (4.34) and Lemma 4.24(f) we have

\[
Q_{r,v}(x) < 4K_3 \exp \left[ \max(-\langle w, z \rangle \log \theta, \zeta_4/K_3) \right], \tag{4.35}
\]

where \( z := c_{\text{in}}^r - c_{\text{in}}^- \). Combining this with Corollary 4.22 and the inequality \( \vartheta^{(w,z)} \leq 1 \) from Lemma 4.24(d), we obtain for \( r \in \mathcal{R}_+ \)

\[
\frac{A_{r,v}(x)}{A_{r-,v}(x)} Q_{r,v}(x) \leq K_2 \frac{\vartheta^{(w,z)}}{\vartheta^{(w,z)}+1} Q_{r,v}(x) < 4K_3 K_3 e^{c_4} =: K_5. \tag{4.36}
\]

For \( r \in \mathcal{R}_0 \), by the same reasoning, now using that \( \delta_j \log \theta = C_2j \) and Lemma 4.24(b) and (c), instead of Lemma 4.24(f) and (d), respectively, we arrive at

\[
\frac{A_{r,v}(x)}{A_{r-,v}(x)} Q_{r,v}(x) < K_5 e^{2c_4 C_{2j}}. \tag{4.37}
\]

Finally, since there are at most \( m \) reactions, (4.36) and (4.37) imply (4.33). \( \square \)

4.1.3 Proof of Theorem 4.9

Fixing \( \mathcal{P} \subseteq \mathcal{S} \) and \( (j, i) \in \mathcal{I}(\mathcal{P})^* \), we consider the open set \( (\mathcal{F}^*)_{c_4} \) for the spherical image \( \mathcal{F}^* \) of the face \( \mathcal{F} = \mathcal{W}(\mathcal{P})_{c_4} \), and proceed to prove (4.14) under our standard conditions, which by Remark 4.17 suffices for proving Theorem 4.9. Requiring that

\[
\max(2c_4, c_4 C_{2j}) \leq K_2 C_{2j+1}, \tag{4.38}
\]
we have already bounded in Corollary 4.26 the LHS of (4.14), so proceed to handle \( r = \mathcal{R}(P)_- \), starting with the case where \( \text{supp} \{ \epsilon_{\text{out}} \} \subseteq \mathcal{P} \). For such a reaction we have by Lemma 4.23, Lemma 4.24 (e) and our choice of \( \varepsilon \) that
\[
Q_{r,\varepsilon}(x) \leq U(x) \left\{ e^{(\langle w, e^- \rangle \log \vartheta + \zeta_\varepsilon)/U(x) - 1} \right\} \\
\leq U(x) \left\{ e^{-K_2 C_{j+1}}/(2U(x)) - 1 \right\}.
\]

Further choosing \( \vartheta_0(C_{2j+1}) \) large enough to have \( 2U(x) \geq K_2 C_{2j+1} \) whenever \( \|x\|_2 \geq \vartheta_0 \) and using that \( e^{-y} - 1 \leq -y/2 \) for \( y \in [0, 1] \), we deduce that for such a reaction
\[
Q_{r,\varepsilon}(x) \leq -\frac{K_2}{4} C_{2j+1}.
\]

Considering Lemma 4.25 for \( K_4 = K_2 C_{2j+1} \) extends (4.39) to \( r \in \mathcal{R}(P)_- \) with \( \text{supp} \{ \epsilon_{\text{out}} \} \subseteq \mathcal{P} \), provided \( \vartheta_0(K_4) \) is large enough. In particular, this proves the negativity of \( Q_{r,\varepsilon}(x) \) which is necessary in order for (4.14) to imply Proposition 4.15. Combining (4.33) and (4.39) we conclude that
\[
\sum_{r \in \mathcal{R}(P)_+ \cup \mathcal{R}(P)_0} \frac{A_{r,w}(\vartheta^w)}{A_{r,\varepsilon}(\vartheta^w)} Q_{r,\varepsilon}(\vartheta^w) < -Q_{r,-\varepsilon}(\vartheta^w),
\]
provided that for \( j = 0, 1, \ldots, d - 1 \),
\[
4m K_6 e^{2 C_{2j}} C_{2j} \leq K_2 C_{2j+1}.
\]

Noting that \( 2 \zeta_\varepsilon \leq 2 e^{\zeta_\varepsilon} \leq K_5 \) and \( c_0 C_{2j} \leq e^{2 C_{2j}}, \) inequality (4.40) guarantees that our preceding requirement (4.38) also holds. In particular, (4.40) allows us to set \( K_0 \) in Def. 4.14 as
\[
K_0 := 4m K_6 / K_2.
\]

Combining this result with the negativity of \( Q_{r,-\varepsilon}(x) \) shown in (4.39) proves (4.13) under our standard conditions. In case the reader worries about the exact order in which the various constants appear in this proof, we start by setting all those constants that depend exclusively on the structure of the network at hand, i.e., \( K_1, \zeta_\varepsilon, \vartheta_0, K_2, K_3 \) and \( K_5 \). These determine \( K_0 \) by (4.41) and consequently all the constants \( \{ C_j \} \) in (4.10) (backwards from \( C_{2d-1} = 1 \)). We then consider Lemma 4.25 for \( K_4 = K_2 C_{2j+1} \) and \( j = 0, \ldots, d_P - 1 \), as well as all other places where \( \vartheta_0 \) is to be enlarged as a function of all the above. Finally, for any \( \vartheta > \vartheta_0 \) we set \( \vartheta^\varepsilon(\vartheta) := \vartheta^\varepsilon \), which in light of Remark 4.17 completes the proof of Theorem 4.39.

**Remark 4.27.** Closer inspection of the proof reveals that the constants \( c_0 \) and \( K_0 \) in Definition 4.14 only depend on the reaction rate constants \( \{ k_j \} \), the dimension \( d \), the minimal angles of the faces of the polyhedron and the maximal value of \( \|c\|_2 \) for \( c \in C \). Our bounds on \( \vartheta_0 \) and \( \vartheta \) are therefore universal and only depend on \( \{ k_j \} \) and on the geometry of the network at hand.
5 Wentzell-Freidlin theory: Some remarks

In this section and the next we deal with some local questions. While large deviations theory is interesting both at large and small concentrations, there is of course the question of what kinds of transitions between stable regimes are possible. For such questions, \( \text{WF} \) theory is adequate. Here, we make contact between these two aspects.

The scope of large deviations estimates can be extended from finite to infinite time intervals through \( \text{WF} \) theory \cite{14}. That framework allows for the asymptotic estimation of the exit time \( \tau_D := \inf \{ t : X_t^\omega \notin D \} \) for sufficiently regular compact domains \( D \subset \mathbb{R}_\omega^d \) (see \cite{1, Ass. A.3}), transition times between attractors and invariant measure densities. The relevant quantity for such estimates is given by the \( \text{WF}-\)quasipotential

\[
V_D(A, B) := \inf_{x \in A, y \in B} \inf_{\tau > 0, z \in \mathcal{AC}_\tau(D)} I_{x,\tau}(z),
\]

for a fixed domain \( D \), any pair of sets \( A, B \subset D \) and \( I(\cdot) \) of \( (3.2) \). This quantity defines a notion of distance between attractors. This can be used to define an equivalence relation between attractors: For a fixed domain \( D \) and a pair of attractors \( A, B \) are equivalent (\( A \sim_D B \)) if \( V_D(A, B) = V_D(B, A) = 0 \).

We will abstain to repeat here the ideas and remaining definitions of \cite{14}. An interesting question is to find criteria where the fundamental assumptions of this theory can really be verified. Indeed, these conditions (summarized in points (a)-(c) of Assumption A.3 below) speak to the post-asymptotic dynamics of the system under study, and there does not appear to be both simple and general conditions allowing to control, even for the relatively limited class of polynomial dynamical systems, the following necessary assumption:

**Assumption A.3** (\cite{1, Ass. A4}). There exist \( \ell \) compact sets \( K_i \subset D \) such that:

(a) every \( \omega \)-limit set of \( (2.3) \) lying entirely in \( D \) is fully contained within one \( K_i \),
(b) for any \( x \in K_i \) we have \( x \sim_D y \) if and only if \( y \in K_i \),
(c) for all \( K_i \), the set \( K_j \) minimizing \( V_D(K_i, K_j) \) is unique.
(d) For every \( c \in \mathbb{R}_\omega^d \), \( c \in \mathbb{R}_\omega^d \).

**Remark 5.1.** We are not aware of a general condition on an arbitrary polynomial vector field for which the points (a) and (b) in Assumption A.3 are satisfied. These points of our assumption form a weaker version of Hilbert’s sixteenth problem (see \cite{22}), whereby having finitely many compact sets \( K_i \) separated by finite potential barriers tolerates the existence of infinitely many attractors. Of course, in two dimensions, the Poincaré-Bendixon theory \cite{13} gives the necessary information. This is also related to the fundamental work of Feinberg \cite{13} who actually spells out conditions which guarantee that the system is on a low-dimensional space. It would be interesting to see if the results in \cite{13} can be expanded in order to account for this kind of dynamical behavior.

This assumption, together with Assumption A.2, is shown in \cite{1} to suffice for large deviations estimates on exit times \( \tau_D \), under some regularity assumptions on \( D \).
The relevant quantity for the exponential in v rate of growth of $\tau_D$, if $D$ contains one stable attractor $A$, is given by the quasipotential $V_D(A, \partial D)$ introduced in (5.1). This quantity can be generalized to account for multiple attractors within $D$ and for estimates of invariant measure densities and transition times between attractors are also based on this quantity. However, such estimates are established in [14] under assumption of compact phase space, that we lack here. Solely under our weaker assumptions, only concentration estimates on the transition times between attractors are possible. In particular, no first- or higher moment estimates of the distribution of transition times between attractors, nor invariant measure estimates are possible, in general, under the sole assumptions given here. The problem is that certain integrability of the hitting time of a compact set is needed for proving such results. Indeed, [2] gives examples of ASE networks not satisfying the integrability condition.

6 Bistable behavior

In this section we introduce an example CRN displaying bi-stable behavior in order to concretely illustrate the results obtained in the previous sections, stressing in particular the extent to which they can or cannot be used.

To stress the generality of the theory developed in this paper, the example introduced in this section has been chosen to display, in one of its attractors, a dynamic behavior that is more exotic than the one observed in examples of bi-stable systems studied in the literature [16,33]. Indeed, we have developed our example CRN based on a system that is known, for a certain choice of reaction rate constants, to display chaotic behavior. This system is inspired by the well known Belusov-Zhabotinski reaction, a naturally occurring set of chemical reactions displaying chaotic and periodic behavior that can be modeled by the following set of chemical reactions [34]:

$$
\emptyset \xrightarrow{k_0} X, \quad X \xrightarrow{k_1} Y, \quad Y \xrightarrow{k_2} Z, \quad Z \xrightarrow{k_3} \emptyset, \quad Z \xrightarrow{k_4} X + Z, \quad X + 2Y \xrightarrow{k_5} 3Y. \quad (6.1)
$$

Despite the fact that the minimality of this system within the set of chemical reaction systems with chaotic dynamics in a non-vanishing region of parameter space has not been proven, some features of this model are strictly necessary (and therefore, in some sense, minimal) for the expected dynamic behavior to occur. For instance, the Poincaré-Bendixson theorem [5] significantly limits the set of possible dynamical landscapes in 2 dimensions, ruling out among other things chaotic trajectories in that dimension and implying the necessity of a phase space of dimension $\geq 3$—as the one of (6.1)—for the observation of chaos.

To induce bi-stability in our model we add a new species, whose interactions are described by the simplest CRN displaying bi-stability [33], universally referred to as the Schlögl model [28]:

$$
\emptyset \xrightarrow{k_v} W, \quad W \xrightarrow{k_a} 2W, \quad W \xrightarrow{k_a} 3W. \quad (6.2)
$$

The two completely independent systems (6.1) and (6.2) can now be coupled through some reactions involving species form both sides:
The choice of these reactions is not casual: As it can be seen in (6.5), the addition of these two reactions effectively shifts the reaction rates constants $k_0$ and $k_4$ by the $w$-dependent amounts $k_{10}w$ and $k_{11}w$. In particular, restricting our attention to the two equilibria $w^*, w^{**}$ of (6.2) (not modified by the addition of the coupling reactions), our system is equivalent to two Belousov-Zhabotinski reactions with

$$k_0 \to k_0^{(i)} := k_0 + k_{10}w^{(i)}, \quad k_4 \to k_4^{(i)} := k_4 + k_{11}w^{(i)}$$

for $i = *, **$, respectively. Therefore, choosing $k_{10}$ and $k_{11}$ appropriately, we obtain a CRN displaying bi-stable behavior between a cycle and a chaotic attractor.

The system resulting from the composition of (6.1), (6.2) and (6.3) satisfies the asiphonic condition (Assumption A.1 (a)) but not the strongly endotactic one (Assumption A.1 (b)): Along directions $n_0 = (-3, 3, 3, 1)$ and $n_1 = (3, 0, 3, 1)$ there is a $n$-explosive reaction in $R_n$ for $n \in \{n_0, n_1\}$. However, the system can be made strongly endotactic by addition of the following reactions:

$$3Y \xrightarrow{k_{12}} \emptyset, \quad X + Z \xrightarrow{k_{13}} X.$$  (6.4)

Remember that the strongly endotactic property guarantees stability of the system in the limit of large $\|x\|_1$, and is indifferent to the dynamic behavior of the system within a compact. This is reflected in the purely topological nature of this condition, which is in particular independent on the reaction rate constants $\{k_r\}_{r \in \mathbb{R}}$. Consequently, the reaction rates of (6.4) can be chosen small enough not to influence, qualitatively, the nature of the (compact) attractors, while ensuring the asymptotic stability and exponential tightness of the system. In Fig. 9 a Poincaré section of one of the attractors of this CRN suggests that its chaotic behavior is indeed not influenced, for our choice of reaction rate constants, by the addition of reactions in (6.4).

To summarize, the system

\[
\begin{align*}
X &\xrightarrow{k_{10}} X + W, \\
Z &\xrightarrow{k_{11}} X + Z + W.
\end{align*}
\]  (6.3)

displays, if modeled stochastically, spontaneous transitions between a chaotic and a cyclic attractor, as displayed in Fig. 10b. Moreover we note that the system respects Assumption A.2 and Assumption A.3 (for large enough $D$). For a specific choice of reaction rate constants, some trajectories of this dynamical system, projected on the $x, y, w$ plane, are displayed in Fig. 10.
Fig. 9: Poincaré section of the $x-y$ projection of the trajectory of the dynamical system (6.5) for the choice of parameters of $k_0 = 2.5, k_1 = 0.0099, k_2 = 1.9851, k_3 = 0.4963, k_4 = 0.0769, k_5 = 0.6352, k_6 = 0.33, k_7 = 2, k_8 = 0.001, k_9 = 0.001, k_{10} = 3, k_{11} = 10^{-9}, k_{12} = 0.01, k_{13} = 10^{-9}$ and $w \equiv w^* = 0.0389$. Assuming the existence of an analytic graph underlying the iterates of the Poincaré map, the associated kneading sequence hints for chaotic behavior of the attractor, conditioned on the negativity of the Schwartzian derivative of the map. This property is stable under small perturbations of the parameters above. The solid black diagonal is the $x = y$ line.

Fig. 10: Projection on the $xzw$-space of simulated deterministic (a) and stochastic (b) dynamics of a multi-attractor system, where one of the attractors is a limit cycle (in blue-green), while the other is a Rössler (chaotic) attractor (in red). In the deterministic case, multiple trajectories have been plotted, with starting points in each of the two basins of attraction. In the stochastic case, a spontaneous transition between the attractors is observed. The parameters of the simulation are those presented in Fig. 9.
6.1 Conclusion - Non-equilibrium quasipotential

We have shown that the stochastic dynamics of certain CRN-s can be studied through large deviations theory, e.g., through [1, Theorems 1.8, 1.9] and that it therefore represents an interesting and dynamically nontrivial example of the reach of this theory. Attention must be paid, though, about the extent of applicability of WF theory to this class of systems. For instance the establishment of first- and higher-moment estimates for the distribution of the transition times between attractors of a CRN as well as exponential estimates on the invariant measure distribution is in general subject to stricter conditions than the ones provided here (c.f. [2]).

The family of large deviations rate functions defined in this paper appeared in the queuing theory literature [11,29,30]. In particular, quantities similar to (3.2) and the corresponding WF-quasipotential are introduced in the context of systems biology as candidates for potential functions in non-equilibrium systems [18,35], where they are used to describe the concentration of the invariant measure $\pi^v(x)$ of a diffusion process $Y^v_t$ approximating $X^v_t$ for $v \to \infty$ over finite time intervals [32]. Furthermore, a Hamilton-Jacobi equation for the analytic calculation of $V(x)$ over the phase space $\mathbb{R}^d$ is derived by studying the first order terms of a WKB expansion of the Fokker-Planck equation for the PDF of the process $Y^v_t$ [15,18,35].

However, the approximation of the process $X^v_t$ through $Y^v_t$ only holds for finite time intervals, while WF estimates extend to infinite time. Furthermore, it is known that, by the different form of the Lagrangian of the LDP for Markov jump and diffusion processes, the exit time and invariant measure estimates predicted by WF-theory will differ, exponentially in $v$, in these two cases [15]. Possible issues arising from the divergence of the WKB expansion as well as existence and uniqueness of the invariant measure for large enough $v$ should also be explicitly addressed, as they might limit the domain of application of the results presented in such papers. In this paper, we have confirmed the partial applicability of such results to systems satisfying Assumptions A.1, A.3, rigorously establishing an LDP in path space with the Lagrangian of Markov Jump processes and extending this result to infinite time intervals through the tools of WF-theory, guaranteeing that $V(x)$ from [14] correctly estimates exit times from compact sets. This suggests that $V$ can be considered as a fundamental quantity for the construction of a non-equilibrium potential.

Still, not all the results of [14] could be established: The existence of an invariant measure and exponential estimates on its concentration as well as the formulation of a HJE for the WF-quasipotential in the case of multiple attractors are not presented in this paper. As shown in [2] there exists a family of ASE networks which lacks the integrability condition to extend the estimates established in this paper to ones of hitting times and of higher moments of the transition times distributions. Another problem is that the function $V$ is in general not everywhere differentiable, preventing its gradient to be a solution to the corresponding HJE, at least in the fully rigorous mathematical sense [8]. Designing clear and general enough boundaries for the applicability of this far-reaching theory, giving solid theoretical grounds to the intuition developed in [35] is an interesting topic for future research.

3 assuming that the set $D$ respects [1, Assumption A.3].
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