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Lyapunov stability of generalized ribosome flows ⋆

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Abstract: In this paper we show that a wide class of compartmental systems with bounded capacities called generalized ribosome flow models are stable with an entropy-like logarithmic Lyapunov function known from the theory of nonnegative systems and reaction networks. The stability proof uses the kinetic representation of the compartmental model and earlier approaches applied for the input-to-state stability analysis of reaction networks with time-varying reaction rates. The results are valid not only for mass action type systems but also for models with more general reaction rates. Illustrative examples are given to show the qualitative dynamical properties of simple generalized ribosome flow models.

Keywords: Lyapunov methods, stability of nonlinear systems, stability of distributed parameter systems, kinetic modeling

1. INTRODUCTION

Nonnegative systems are widely used in several application fields such as chemistry, biology, ecology or transportation, where the described quantities are naturally positive or nonnegative (Haddad et al., 2010). The main mathematical property of such models is that the nonnegative orthant is invariant with respect to the system dynamics. Compartmental models are used to describe the change of the distribution of objects such as molecules, particles, individuals or vehicles among different storage compartments in time (Jacquez and Simon, 1993). Compartments can be physically distinct subsystems such as interconnected containers (e.g., different habitats in ecological models, organs in pharmacokinetics, or road segments in traffic models), but they can also represent disjoint states of a process like different stages of diseases in the case of epidemic models.

The class of kinetic systems (also called reaction networks or simply CRNs) is also an interesting and important part of nonnegative models (Feinberg, 2019). The dynamics of these systems can be formally realized by a set of (generalized) chemical reactions giving rise naturally to a directed graph structure called the reaction graph. Kinetic systems may possess complex dynamical behaviour including multiple equilibria, oscillations, limit cycles or even chaos, therefore, they can be considered as universal descriptors of nonlinear dynamics (Érdi and Tóth, 1989). On the other hand, their mathematical structure is simple enough to develop efficient computational techniques for dynamical analysis and control (Lipták et al., 2016). It is also well-known that majority of compartmental models can be given in kinetic form. Stability analysis has been in the focus of reaction network theory for more than 50 years. In (Horn and Jackson, 1972), a logarithmic function, called pseudo-Helmholtz function is proposed for the stability analysis of a class of CRNs. This function was further generalized, for example in (Lu et al., 2021) using a Lyapunov function PDE approach, for some additional classes of CRNs governed by mass-action kinetics. The well-known deficiency zero theorem was published in (Feinberg, 1987) which states the existence of at least locally stable positive equlibria for weakly reversible CRNs having zero deficiency. The so-called Global Attractor Conjecture says that this stability is actually global with respect to the nonnegative orthant (Craciun, 2015). In (Alonso and Szederkényi, 2016) a new model parametrization approach was given for the study of the uniqueness and stability of equilibria in CRNs with mass action kinetics. In the present paper, we will rely on the basic ideas and the generalized logarithmic Lyapunov function proposed in (Chaves, 2005) for the stability analysis of deficiency zero CRNs with time varying rate coefficients, although the system class we study is not deficiency zero.

Ribosome flow models were introduced to support the dynamical modeling of the gene translation process using the simple exclusion principle and mean field approximation (Reuveni et al., 2011). These models can also be interpreted as kinetic systems having mass action type reaction rates. In (Margaliot and Tuller, 2012) it was shown that ribosome flow models with a tubular structure have unique positive equlibria within each stoichiometric compatibility class, and every trajectory converges to this equilibrium. A

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closed circular ribosome flow model was studied in (Raveh et al., 2015), and it was proved that the system admits a continuum of semistable equlibria. However, to the best of our knowledge, the stability of ribosome flow models has not been studied using entropy-like Lyapunov functions.

The compartmental model class studied in this paper was originally motivated by a special finite volume discretization of traffic flow models proposed in (Lipták et al., 2021), where it was shown that the process has a physically meaningful kinetic interpretation with 'chemical' reactions representing the movement of vehicles between adjacent road cells. In (Szederkényi et al., 2022) this compartmental traffic model was generalized both in terms of structure and kinetics, and the persistence and ℓ_1-contraction property of the dynamics of strongly connected networks was proved. Since this system class includes ribosome flow models mentioned above, in (Vághy and Szederkényi, 2022) the term 'generalized ribosome flow model' was used, and a port-Hamiltonian description reflecting the directed graph structure was given. In the light of the above results, the aim of this paper is to perform the stability analysis of generalized ribosome flow models using an entropy-like Lyapunov function candidate.

2. NOTATIONS AND BACKGROUND

2.1 Compartmental models

The notations and overview in this section are based on (Szederkényi et al., 2022) and (Vághy and Szederkényi, 2022). Throughout the paper we consider systems containing a set of interconnected compartments and objects (such as ribosomes, particles, molecules, vehicles etc.) moving between them. We assume that the rate of transfer between compartments depends on the amount of objects in the source compartment as well as on the amount of free space in the target compartment. This naturally implies that each compartment has a well-defined finite *capacity* that limits the number of items that can be contained in the given compartment.

For the formal definition, let us consider the set $Q = \{q_1, q_2, \ldots, q_m\}$ of compartments and the set $A \subset Q \times Q$ of transitions, where $(q_i, q_j) \in A$ represents the transition from compartment q_i into q_j. Then, the directed graph $D = (Q, A)$ is called *compartmental graph* and it describes the structure of the compartmental model. Loop edges are not allowed in the model. Similarly, we do not allow parallel edges between two compartments in the same direction.

Let $I_m = \{1, 2, \ldots, m\}$. For each compartment q_i we introduce the sets of *donors* and *receptors*, respectively, as

$$\mathcal{D}_i = \big\{ j \in I_m \big| (q_j, q_i) \in A \big\},$$
$$\mathcal{R}_i = \big\{ j \in I_m \big| (q_i, q_j) \in A \big\};$$

that is, the set of donors of a given compartment are the compartments where an incoming transition originates from and the set of receptors are the compartments where an outgoing transition terminates in.

2.2 Chemical reaction networks (kinetic systems)

In this subsection we give a brief introduction of kinetic systems based on (Feinberg, 2019; Horn and Jackson, 1972). A CRN contains a set of *species* $\Sigma = \{X_1, X_2, \ldots, X_N\}$ and the corresponding species vector is given by $X = [X_1\ X_2\ \ldots\ X_N]^{\mathrm{T}}$. The species of a CRN are transformed into each other through *elementary reaction steps* of the form

$$C_j \xrightarrow{\mathcal{K}_j} C_{j'} \qquad j = 1, 2, \ldots, R,$$

where $C_j = y_j^{\mathrm{T}} X$ and $C_{j'} = y_{j'}^{\mathrm{T}} X$ are the source and product *complexes*, respectively, the vectors $y_j, y_{j'} \in \mathbb{N}_0^N$ are *stoichiometric coefficient vectors* and the continuously differentiable functions $\mathcal{K}_j : \overline{\mathbb{R}}_+^N \mapsto \overline{\mathbb{R}}_+$ are the *rate functions* with $\overline{\mathbb{R}}_+$ denoting the set of nonnegative real numbers.

Let $x(t) \in \overline{\mathbb{R}}_+^N$ denote the state vector of the species as a function of time for $t \geq 0$. Based on the above, the dynamics of the CRN is given by

$$\dot{x}(t) = \sum_{j=1}^{R} \mathcal{K}_j(x)[y_{j'} - y_j]. \tag{1}$$

We say that $k \in \mathrm{supp}(y_j)$ if $[y_j]_k > 0$. For the rate functions, we assume the following:

A1 $\frac{\partial K_j(x)}{\partial x_k} \geq 0$ if $k \in \mathrm{supp}(y_j)$ and $\frac{\partial K_j(x)}{\partial x_k} = 0$ if $k \notin \mathrm{supp}(y_j)$,

A2 $K_j\big(x(t)\big) = 0$ whenever there exists $k \in \mathrm{supp}(y_j)$ such that $x_k(t) = 0$.

These assumptions not only guarantee local existence and uniqueness but the invariance of the nonnegative orthant (or a part of it) as well. A set of ODEs of the form $\dot{x} = f(x)$ is called kinetic if it can be written in the form (1) with appropriate rate functions and stoichiometric coefficient vectors.

3. DYNAMICS OF THE STUDIED COMPARTMENTAL MODELS

3.1 Kinetic description

We construct a CRN corresponding to a compartmental model $D = (Q, A)$. Let the set of species be $\Sigma = \{N_1, N_2, \ldots, N_m\} \cup \{S_1, S_2, \ldots, S_m\}$ where N_i and S_i represent the number of particles and available spaces in compartment q_i, respectively. To each transition $(q_i, q_j) \in A$ we assign a reaction of the form

$$N_i + S_j \xrightarrow{\mathcal{K}_{ij}} N_j + S_i,$$

where $\mathcal{K}_{ij}$ is the rate function of the transition. Such a reaction represents that during the transition from compartment q_i to compartment q_j the number of items decreases in q_i and increases in q_j, while the number of available spaces increases in q_i and decreases in q_j. Let n_i and s_i denote the continuous concentration of particles and free spaces in q_i, respectively. Since the rate of the transition $(q_i, q_j) \in A$ only depends on the number of items in compartment q_i and the number of available spaces in compartment q_j, for the sake of simpler notations, we will explicitly write out the arguments as $\mathcal{K}_{ij}(n_i, s_j)$.

Based on (1) the dynamics of the system is given by

$$\begin{aligned}\dot{n}_i &= \sum_{j\in\mathcal{D}_i}\mathcal{K}_{ji}(n_j,s_i) - \sum_{j\in\mathcal{R}_i}\mathcal{K}_{ij}(n_i,s_j),\\ \dot{s}_i &= -\sum_{j\in\mathcal{D}_i}\mathcal{K}_{ji}(n_j,s_i) + \sum_{j\in\mathcal{R}_i}\mathcal{K}_{ij}(n_i,s_j).\end{aligned} \tag{2}$$

It is easy to check that the model class in Eq. (2) contains ribosome flow models described in (Margaliot and Tuller, 2012) or (Bar-Shalom et al., 2020), and extends them in two ways: firstly, the reaction rate function $\mathcal{K}$ is not necessarily mass action type but more general, and secondly, the compartmental graph of the system can be arbitrary (i.e., there can be particle transition between any two compartments). Therefore, we call (2) a *generalized ribosome flow model*.

3.2 Linear conservation laws

System (2) exhibits conservation in several senses. First of all, we have that

$$\sum_{i=1}^{m}\left(\dot{n}_i + \dot{s}_i\right) = 0,$$

thus the function $H:\mathbb{R}^{2m}\mapsto\mathbb{R}$, given by

$$H(x) = \sum_{i=1}^{2m} x_i,$$

for $x\in\mathbb{R}^{2m}$ is a first integral and is constant along the trajectories of (2). Our next observation is that $\dot{n}_i + \dot{s}_i = 0$ holds for each compartment, thus $c_i := n_i + s_i$ is the constant capacity of compartment q_i. Substituting $s_i = c_i - n_i$ we can rewrite (2) in a reduced state space as

$$\dot{n}_i = \sum_{j\in\mathcal{D}_i}\mathcal{K}_{ji}(n_j, c_i - n_i) - \sum_{j\in\mathcal{R}_i}\mathcal{K}_{ij}(n_i, c_j - n_j) \tag{3}$$

or after an analogous substitution, as

$$\dot{s}_i = -\sum_{j\in\mathcal{D}_i}\mathcal{K}_{ji}(c_j - s_j, s_i) + \sum_{j\in\mathcal{R}_i}\mathcal{K}_{ij}(c_i - s_i, s_j). \tag{4}$$

As a consequence of the preceding observations, the function $\tilde{H}:\mathbb{R}^m\mapsto\mathbb{R}$, given by

$$\tilde{H}(x) = \sum_{i=1}^{m} x_i$$

for $x\in\mathbb{R}^m$ is a first integral for (3) and (4) with $x = n$ and $x = s$, respectively. This shows that while the state space of the decomposed systems is $\tilde{C} := [0,c_1]\times[0,c_2]\times\cdots\times[0,c_m]$, for a given initial condition $x(0)\in\mathbb{R}^m$ the trajectories are contained in the $(m-1)$-dimensional manifold (hyperplane) defined by

$$\left\{x\in\tilde{C}\middle|\tilde{H}(x) - \tilde{H}\big(x(0)\big) = 0\right\}.$$

Similarly, in the original state space $C := \tilde{C}\times\tilde{C}$, for a given initial condition $x(0)\in C$ the trajectory is contained in the $(m-1)$-dimensional manifold (hyperplane) defined by

$$\begin{aligned}\Big\{x\in C\Big|c_i - (x_i + x_{m+i}) = 0 \text{ for } i = 1,2,\ldots,m;\\ H(x) - H\big(x(0)\big) = 0\Big\},\end{aligned}$$

where the local coordinates $x_1,\ldots,x_m$ and $x_{m+1},\ldots,x_{2m}$ correspond to the variables $n_1,\ldots,n_m$ and $s_1,\ldots,s_m$, respectively.

3.3 Qualitative dynamical properties

We recall the following theorem about the qualitative behaviour of the studied compartmental models.

Theorem 1. (Szederkényi et al. (2022)). For a strongly connected compartmental graph the corresponding CRN given in (2) has the following properties:

(i) Its dynamics is persistent; that is, for each $x(0)\in\operatorname{int}(C)$ we have that $\omega\big(x(0)\big)\cap\partial C = \emptyset$.
(ii) For each $x(0)\in C$ the orbit enters $\operatorname{int}(C)$ after an arbitrarily short time and never leaves it.
(iii) Each level set of the first integral H has exactly one equilibrium that attracts the whole level set.

In this paper we assume that the reaction rate of the transition (q_i,q_j) is of the form $\mathcal{K}_{ij}(n_i,s_j) = k_{ij}\theta_i(n_i)\nu_j(s_j)$, where $k_{ij}>0$ and $\theta_i,\nu_j\in\mathcal{C}^1(\mathbb{R})$ are nondecreasing, have $\theta_i(0) = \nu_j(0) = 0$ and satisfy $\int_0^1|\log\theta_i(r)|\,\mathrm{d}r < \infty$ and $\int_0^1|\log\nu_j(r)|\,\mathrm{d}r < \infty$. It is easy to see that the assumptions **A1** and **A2** on the reaction rates given in subsection 2.2 are satisfied in this case, and thus Theorem 1 holds.

4. STABILITY ANALYSIS

We rewrite the state-space model (2) as a system of ODEs of the form of (1). In order to do so, let $x\in\mathbb{R}^{2m}$ be such that $x_i = n_i$ and $x_{m+i} = s_i$ for $i = 1,2,\ldots,m$. Define the functions $\gamma_i = \theta_i$ and $\gamma_{m+i} = \nu_i$ for $i = 1,2,\ldots,m$. Denote the number of complexes in the assigned CRN with M and let y_i be the stoichiometric coefficient vector of complex C_i for $i = 1,2,\ldots,M$. For the sake of brevity, let $\gamma^{y_i}(x) = \prod_{l=1}^{2m}\gamma_l^{y_{i,l}}(x_l)$. Equilibrium points in the state space are denoted by $\overline{x}$. Finally, let $k_{ij} = 0$ if $(q_i,q_j)\notin A$. Using these notations rewrite (2) as follows:

$$\dot{x} = \sum_{i=1}^{M}\sum_{j=1}^{M} k_{ij}\gamma^{y_i}(x)(y_j - y_i). \tag{5}$$

We consider the following entropy-like function (Chaves, 2005; Feinberg, 2019; Sontag, 2001):

$$V(x,\overline{x}) = \sum_{i=1}^{2m}\int_{\overline{x}_i}^{x_i}\big(\log\gamma_i(s) - \log\gamma_i(\overline{x}_i)\big)\,\mathrm{d}s$$

and proceed by showing that it is a Lyapunov function for (5). In the subsequent analysis we assume that $\overline{x}$ is positive, which, for example, is ensured by Theorem 1 if the compartmental graph is strongly connected.

A transformation of special interest is the case $\gamma_i(r) = r$. This corresponds to the law of mass action; that is, in this case $\mathcal{K}_{ij}(n_i,s_j) = k_{ij}n_is_j$. Furthermore, since

$$\int_{\overline{x}_i}^{x_i}\big(\log\gamma_i(s) - \log\gamma_i(\overline{x}_i)\big)\,\mathrm{d}s = x_i\log\frac{x_i}{\overline{x}_i} + \overline{x}_i - x_i$$

the Lyapunov function candidate can be written explicitly as

$$V(x,\overline{x}) = \sum_{i=1}^{2m}\left(x_i\log\frac{x_i}{\overline{x}_i} + \overline{x}_i - x_i\right). \tag{6}$$

Another important example from (bio)chemistry is a reaction rate in rational form, which is given as $\gamma_i(r) = \frac{r}{k+r}$ for some $k>0$. This functions describes reaction rates with

saturation; that is, we have that $\gamma_i(r) \to 1$ as $r \to \infty$. In this case, too, the integral can be calculated analytically and we can rewrite the Lyapunov function candidate as

$$V(x,\overline{x}) = \sum_{i=1}^{2m} \left((k + x_i) \log \frac{k + \overline{x}_i}{k + x_i} + x_i \log \frac{x_i}{\overline{x}_i} \right). \quad (7)$$

Let $\rho(x) = \left[\log \gamma_1(x_1) \ \log \gamma_2(x_2) \ \cdots \ \log \gamma_{2m}(x_{2m})\right]^{\mathrm{T}}$ and and $q_i = \langle y_i, \rho(x) - \rho(\overline{x}) \rangle$. Note, that $\nabla V(x,\overline{x}) = \rho(x) - \rho(\overline{x})$. Using this, we obtain

$$\begin{aligned} \dot{V}(x,\overline{x}) &= \langle \nabla V, \dot{x} \rangle \\ &= \sum_{i=1}^{M} \sum_{j=1}^{M} k_{ij} \gamma^{y_i}(x) \langle \rho(x) - \rho(\overline{x}), y_j - y_i \rangle \\ &\sum_{i=1}^{M} \sum_{j=1}^{M} k_{ij} \gamma^{y_i}(x)(q_j - q_i). \end{aligned} \quad (8)$$

Notice, that

$$\gamma^{y_i}(x) = e^{\langle y_i, \rho(x) \rangle} = e^{\langle y_i, \rho(\overline{x}) \rangle} e^{q_i}$$

thus (8) can be rewritten as

$$\dot{V}(x,\overline{x}) = \sum_{i=1}^{M} \sum_{j=1}^{M} k_{ij} e^{\langle y_i, \rho(\overline{x}) \rangle} e^{q_i} (q_j - q_i). \quad (9)$$

Using

$$\begin{aligned} e^{q_i}(q_j - q_i) &= e^{q_i}(q_j - q_i) - e^{q_i}(e^{q_j - q_i} - 1) \\ &\quad + e^{q_i}(e^{q_j - q_i} - 1) \\ &= e^{q_i}\big((q_j - q_i) - e^{q_j - q_i} + 1\big) + e^{q_j} - e^{q_i} \\ &= -e^{q_i}\big(e^{q_j - q_i} - (q_j - q_i) - 1\big) + e^{q_j} - e^{q_i} \\ &= -e^{q_i}\omega(q_j - q_i) + e^{q_j} - e^{q_i} \end{aligned}$$

where $\omega(r) = e^r - r - 1$, further rewrite (9) as

$$\begin{aligned} \dot{V}(x,\overline{x}) = &- \sum_{i=1}^{M} \sum_{j=1}^{M} k_{ij} e^{\langle y_i, \rho(\overline{x}) \rangle} e^{q_i} \omega(q_j - q_i) \\ &+ \sum_{i=1}^{M} \sum_{j=1}^{M} k_{ij} e^{\langle y_i, \rho(\overline{x}) \rangle} (e^{q_j} - e^{q_i}). \end{aligned}$$

Focusing on the second term we have that

$$\begin{aligned} &\sum_{i=1}^{M} \sum_{j=1}^{M} k_{ij} e^{\langle y_i, \rho(\overline{x}) \rangle} (e^{q_j} - e^{q_i}) \\ &= \sum_{j=1}^{M} e^{q_j} \left(\sum_{i=1}^{M} k_{ij} e^{\langle y_i, \rho(\overline{x}) \rangle} \right) - \sum_{i=1}^{M} e^{q_i} \left(\sum_{j=1}^{M} k_{ij} \right) e^{\langle y_i, \rho(\overline{x}) \rangle} \end{aligned}$$

Let $Y = [y_1 \ y_2 \ \cdots \ y_M]$ be the stoichiometric matrix and K be the weighted adjacency matrix of the reaction graph of the CRN. Finally, introduce $Q = \left[e^{q_1} \ e^{q_2} \ \cdots \ e^{q_M}\right]$ to find that

$$\begin{aligned} &\sum_{i=1}^{M} \sum_{j=1}^{M} k_{ij} e^{\langle y_i, \rho(\overline{x}) \rangle} (e^{q_j} - e^{q_i}) \\ &= QKe^{Y^{\mathrm{T}}\rho(\overline{x})} - Q\mathrm{diag}\big(1_{2m}^{\mathrm{T}} K\big) e^{Y^{\mathrm{T}}\rho(\overline{x})} \\ &= Q\Big(K - \mathrm{diag}\big(1_{2m}^{\mathrm{T}} K\big)\Big) e^{Y^{\mathrm{T}}\rho(\overline{x})} = Q\tilde{K} e^{Y^{\mathrm{T}}\rho(\overline{x})} \end{aligned} \quad (10)$$

where $\tilde{K}$ is the weighted negative Laplacian of the reaction graph. Recall that (5) is equivalent to

$$\dot{x} = Y\tilde{K} e^{Y^{\mathrm{T}}\rho(x)}$$

and that at equilibrium

$$Y\tilde{K} e^{Y^{\mathrm{T}}\rho(\overline{x})} = 0.$$

Since Y is of full rank (since each complex is unique, second order and contains two different species), we have that $\tilde{K} e^{Y^{\mathrm{T}}\rho(\overline{x})} = 0$, and thus (10) is zero. This shows that

$$\dot{V}(x,\overline{x}) = -\sum_{i=1}^{M} \sum_{j=1}^{M} k_{ij} e^{\langle y_i, \rho(\overline{x}) \rangle} e^{q_i} \omega(q_j - q_i) =: -W(x,\overline{x}).$$

We know that $k_{ij} \geq 0$, $e^{\langle y_i, \rho(\overline{x}) \rangle} > 0$ and $e^{q_i} > 0$. Finally, we can observe that $\omega(r) = e^r - r - 1 \geq 0$ and $\omega(r) = 0$ if and only if $r = 0$, and thus

$$\dot{V}(x,\overline{x}) = -W(x,\overline{x}) \leq 0$$

and $\dot{V}(x,\overline{x}) = 0$ if and only if $x = \overline{x}$ and the proof is finished.

Remark 2. Note, that we did not use any structural properties of K or $\tilde{K}$, in particular, we did not rely on the fact that the compartmental graph is strongly connected. We would only need strong connectivity to ensure the existence of a unique positive equilibrium point by the virtue of Theorem 1. In fact, if for example the initial state and the capacities guarantee that no compartment can become empty, then our proof ensures Lyapunov stability, see Example 5.2.

5. EXAMPLES

5.1 A strongly connected network

Consider a compartmental model with $Q = \{q_1, q_2, q_3\}$ and $A = \big\{(q_1, q_2), (q_2, q_3), (q_3, q_1)\big\}$. The directed graph $D = (Q, A)$ is strongly connected, see Figure 1.

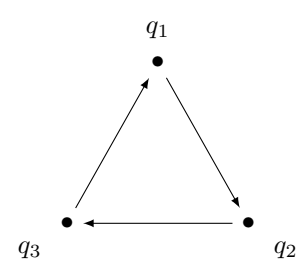

Fig. 1. Compartmental graph of a strongly connected model

The corresponding chemical reaction network has species $\Sigma = \{N_1, N_2, N_3, S_1, S_2, S_3\}$ and consists of the following reactions:

$$\begin{aligned} N_1 + S_2 &\xrightarrow{\mathcal{K}_{12}} N_2 + S_1 \\ N_2 + S_3 &\xrightarrow{\mathcal{K}_{23}} N_3 + S_2 \\ N_3 + S_1 &\xrightarrow{\mathcal{K}_{31}} N_1 + S_3 \end{aligned}$$

Indeed, the reaction graph is not strongly connected and not weakly reversible. According to (3), the dynamics of the system in the reduced state space can be given as

$$
\begin{aligned}
\dot{n}_1 &= \mathcal{K}_{31}(n_3, c_1 - n_1) - \mathcal{K}_{12}(n_1, c_2 - n_2) \\
&= k_{31}\theta_3(n_3)\nu_1(c_1 - n_1) - k_{12}\theta_1(n_1)\nu_2(c_2 - n_2) \\
\dot{n}_2 &= \mathcal{K}_{12}(n_1, c_2 - n_2) - \mathcal{K}_{23}(n_2, c_3 - n_3) \\
&= k_{12}\theta_1(n_1)\nu_2(c_2 - n_2) - k_{23}\theta_2(n_2)\nu_3(c_3 - n_3) \\
\dot{n}_3 &= \mathcal{K}_{23}(n_2, c_3 - n_3) - \mathcal{K}_{31}(n_3, c_1 - n_1) \\
&= k_{23}\theta_2(n_2)\nu_3(c_3 - n_3) - k_{31}\theta_3(n_3)\nu_1(c_1 - n_1).
\end{aligned}
$$

For the following simulations we set the capacities as $c_1 = c_2 = c_3 = 100$ and the reaction rate coefficients as $k_{12} = 100$, $k_{23} = 60$ and $k_{31} = 20$.

Mass action kinetics Let us assume that the rate functions are of the mass action type; that is, each transformation has the form $\gamma_i(r) = r$, and thus each $\mathcal{K}_{ij}(n_i, s_j) = k_{ij} n_i s_j$. Figure 2 shows the level set of the first integral $\{x \in C \big| H(x) = 150\}$ and its unique equilibrium, along with some orbits on the level set. The (n_1, n_2) plane contains the (filled) level curves of the Lyapunov function in (6), which, considering the conservation $H(n) = 150$, can be viewed as a function of two variables.

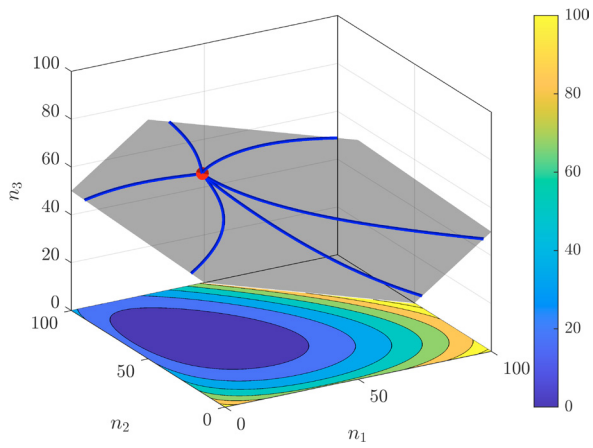

Fig. 2. Phase portrait of a strongly connected compartmental model with mass action kinetics

Figure 3 shows the level curves of the Lyapunov function along with the vector field $[\dot{n}_1, \ \dot{n}_2]^{\mathrm{T}}$ and the unique equilibrium of the level set.

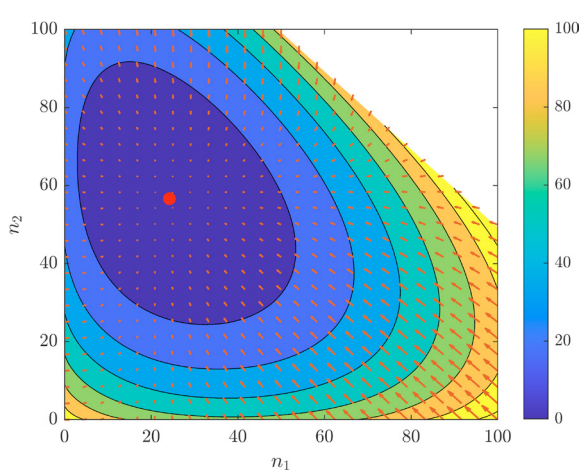

Fig. 3. Level curves of the Lyapunov function (6) for a strongly connected system with mass action kinetics

Rational kinetics In this example we assume that each transformation has the rational form $\gamma_i(r) = \frac{r}{k+r}$ with $k = 50$. Figures 4 and 5 show the phase portrait and level curves of the Lyapunov function in a similar manner as before.

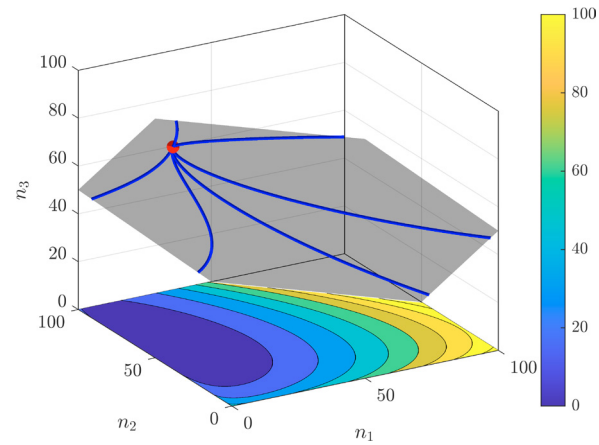

Fig. 4. Phase portrait of a strongly connected compartmental model with rational kinetics

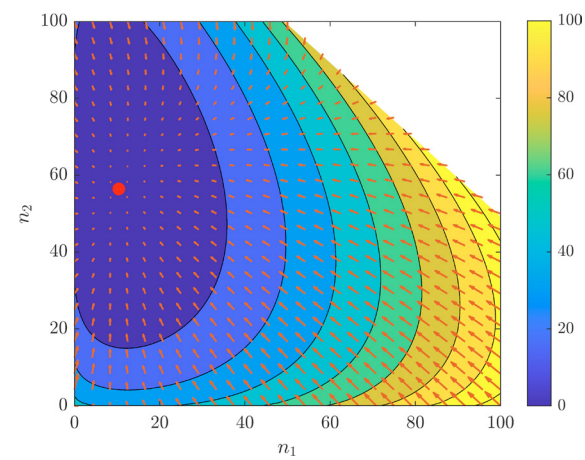

Fig. 5. Level curves of the Lyapunov function (7) for a strongly connected system with rational kinetics

5.2 General network topology

In this example we consider a compartmental model with $Q = \{q_1, q_2, q_3\}$ and $A = \{(q_2, q_3), (q_3, q_1), (q_3, q_2)\}$. The directed graph $D = (Q, A)$ in this case is not strongly connected, see Figure 6.

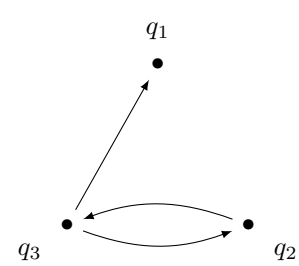

Fig. 6. Compartmental graph of a not strongly connected model

In this case, too, the reaction graph is not strongly connected and not weakly reversible. According to (3), the

dynamics of the system in the reduced state space can be given as

$$\begin{aligned}\dot{n}_1 &= k_{31}\theta_3(n_3)\nu_1(c_1 - n_1)\\ \dot{n}_2 &= k_{32}\theta_3(n_3)\nu_2(c_2 - n_2) - k_{23}\theta_2(n_2)\nu_3(c_3 - n_3)\\ \dot{n}_3 &= k_{23}\theta_2(n_2)\nu_3(c_3 - n_3) - k_{31}\theta_3(n_3)\nu_1(c_1 - n_1)\\ &\quad - k_{32}\theta_3(n_3)\nu_2(c_2 - n_2).\end{aligned}$$

We consider rational kinetics with capacities and reaction rate coefficients as before and $k = 50$. Notice, that $\dot{n}_1(t) = 0$ for some $t \geq 0$ implies $n_1(t) = c_1$ or $n_3(t) = 0$, but $n_3(t) = 0$ cannot happen as long as $n_2(t) > 0$. Thus, on the level set corresponding to a total mass of 150, there exists a unique equilibrium with $\overline{n}_1 = c_1 = 100$, i.e. the compartment q_1 gets saturated. The remaining subsystem (q_2, q_3) is strongly connected, and thus by Theorem 1 the equilibrium is positive. Figures 7 and 8 show the phase portrait of the system and the level curves of the Lyapunov function.

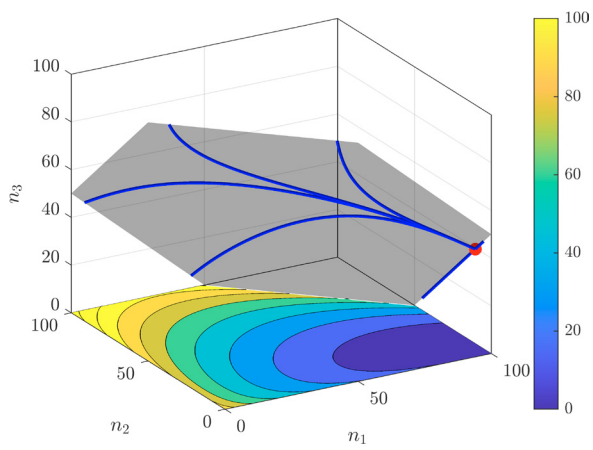

Fig. 7. Phase portrait of a not strongly connected compartmental model with rational kinetics

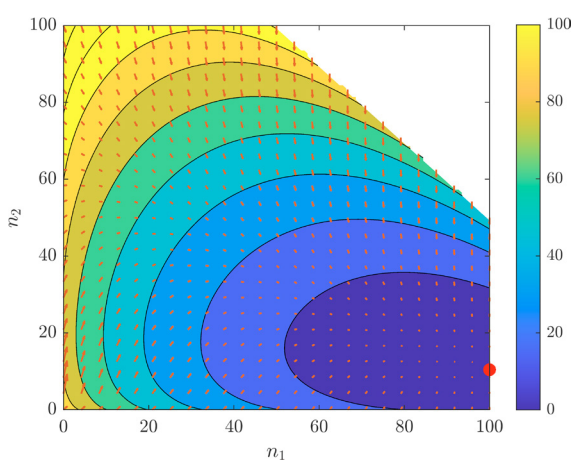

Fig. 8. Level curves of the Lyapunov function (7) for a not strongly connected compartmental model with rational kinetics

6. CONCLUSIONS

In this paper we investigated a class of compartmental models called generalized ribosome flows. Using the kinetic representation we showed that the positive equilibria are stable with a logarithmic Lyapunov function well-known from the theory of reaction networks. The results are applicable to a wide class of reaction rate functions including mass action kinetics. The qualitative properties of generalized ribosome flows were illustrated on small examples. In particular, a model with not strongly connected compartmental topology was investigated, where the graph structure and the initial values ensured the existence of a positive equilibrium. Motivated by these results, our further plans include the analysis of more general compartmental graphs and the application of Lyapunov stability in control problems.

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