Chapter 3
Guaranteeing Spatial Uniformity in Reaction-Diffusion Systems Using Weighted L^2 Norm Contractions

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Abstract We present conditions that guarantee spatial uniformity of the solutions of reaction-diffusion partial differential equations. These equations are of central importance to several diverse application fields concerned with pattern formation. The conditions make use of the Jacobian matrix and Neumann eigenvalues of elliptic operators on the given spatial domain. We present analogous conditions that apply to the solutions of diffusively-coupled networks of ordinary differential equations. We derive numerical tests making use of linear matrix inequalities that are useful in certifying these conditions. We discuss examples relevant to enzymatic cell signaling and biological oscillators. From a systems biology perspective, the paper's main contributions are unified verifiable relaxed conditions that guarantee spatial uniformity of biological processes.

Keywords Reaction-diffusion systems · Turing phenomenon · Diffusive instabilities · Compartmental systems · Contraction methods for stability · Matrix measures

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3.1 Introduction

This paper studies reaction-diffusion partial differential equations (PDEs) of the form

$$\frac{\partial u}{\partial t}(\omega, t) = F(u(\omega, t), t) + \mathcal{L}u(\omega, t), \tag{3.1}$$

where $\mathcal{L}$ denotes a diffusion operator. We prove a two-part result that addresses the question of how the stability of solutions of the PDE relates to stability of solutions of the underlying ordinary differential equation (ODE) $\frac{dx}{dt}(t) = F(x(t), t)$. The study of this question is central to many application fields concerned with pattern formation, ranging from biology (morphogenesis developmental biology, species competition and cooperation in ecology, epidemiology) [8, 9, 23] and enzymatic reactions in chemical engineering [24] to spatio-temporal dynamics in semiconductors [21].

The first part of our result shows that when solutions of the ODE have a certain contraction property, namely $\mu_{2,Q}(J_F(u,t)) < 0$ uniformly on u and t, where $\mu_{2,Q}$ is a logarithmic norm (matrix measure) associated to a Q-weighted L^2 norm, the associated PDE, subject to no-flux (Neumann) boundary conditions, enjoys a similar property. This result complements a similar result shown in [1] which, while allowing norms L^p with p not necessarily equal to 2, had the restriction that it only applied to diagonal matrices Q and $\mathcal{L}$ was the standard Laplacian. Logarithmic norm or "contraction" approaches arose in the dynamical systems literature [12, 15, 17], and were extended and much further developed in work by Slotine e.g. [16]; see also [18] for historical comments.

The second, and complementary, part of our result shows that when $\mu_{2,Q}(J_f(u,t) - \Lambda_2) < 0$, where Λ_2 is a nonnegative diagonal matrix whose entries are the second smallest Neumann eigenvalues of the diffusion operators in (1), the solutions become spatially homogeneous as $t \to \infty$. This result generalizes the previous work [3] to allow for spatially-varying diffusion, and makes a contraction principle implicitly used in [3] explicit.

We next turn to compartmental ordinary differential equations (ODEs), where each compartment represents a well-mixed spatial domain wherein corresponding components in adjacent compartments are coupled by diffusion [11], and present spatial uniformity conditions analogous to those derived for the PDE case. We then derive convex linear matrix inequality [4] tests as in [3] that can be used to certify the conditions. Our discussion is punctuated by several examples of biological interest.

3.2 Spatial Uniformity in Reaction-Diffusion PDEs

In this section, we study the reaction-diffusion PDE (3.1), subject to a Neumann boundary condition:

$$\nabla u_i \cdot \mathbf{n}(\xi, t) = 0 \quad \forall \xi \in \partial\Omega, \quad \forall t \in [0, \infty). \tag{3.2}$$

Assumption 1 In (3.1)–(3.2) we assume:

- Ω is a bounded domain in $\mathbb{R}^m$ with smooth boundary $\partial\Omega$ and outward normal $\mathbf{n}$.
- $F\colon V \times [0, \infty) \to \mathbb{R}^n$ is a (globally) Lipschitz and twice continuously differentiable vector field with respect to x, and continuous with respect to t, with components F_i:
$$F(x, t) = (F_1(x, t), \ldots, F_n(x, t))^T$$
for some functions $F_i\colon V \times [0, \infty) \to \mathbb{R}$, where V is a convex subset of $\mathbb{R}^n$.
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$$\mathcal{L} = \text{diag}\,(\mathcal{L}_1, \ldots, \mathcal{L}_n)\,, \quad \text{and} \quad \mathcal{L}u = (\mathcal{L}_1 u_1, \ldots, \mathcal{L}_n u_n)^T,$$
where for each $i = 1, \ldots, n$,
$$(\mathcal{L}_i u_i)(\omega, t) \;=\; \nabla \cdot (A_i(\omega) \nabla u_i(\omega, t))\,, \tag{3.3}$$
and $A_i\colon \Omega \to \mathbb{R}^{m\times m}$ is symmetric and there exist $\alpha_i, \beta_i > 0$ such that for all $\omega \in \Omega$ and $\zeta = (\zeta_1, \ldots, \zeta_m)^T \in \mathbb{R}^m$,
$$\alpha_i |\zeta|^2 \;\le\; \zeta^T A_i(\omega)\zeta \;\le\; \beta_i |\zeta|^2. \tag{3.4}$$

Suppose that $\mathcal{L}$ has $r \le n$ distinct elements $\mathbf{L}_1, \ldots, \mathbf{L}_r$ (up to a scalar). Namely,

$$\begin{aligned}\text{diag}\left(\mathcal{L}_1, \ldots, \mathcal{L}_{n_1}, \ldots, \mathcal{L}_{n-n_r+1}, \ldots, \mathcal{L}_n\right) &= \\ \text{diag}\left(d_{11}, \ldots, d_{1n_1}, \ldots, d_{r1}, \ldots, d_{rn_r}\right) &\text{diag}\,(\mathbf{L}_1, \ldots, \mathbf{L}_1, \ldots, \mathbf{L}_r, \ldots, \mathbf{L}_r)\,,\end{aligned}$$

where $n_1 + \cdots + n_r = n$. For each $i = 1, \ldots, r$, let D_i be an $n \times n$ diagonal matrix with entries $[D_i]_{n_{i-1}+j, n_{i-1}+j} = d_{ij}$, for $j = 1, \ldots, n_i$, $n_0 = 0$ elsewhere. Also for each $i = 1, \ldots, r$, let $\mathfrak{L}_i$ be an $n \times n$ diagonal matrix with identical entries $\mathbf{L}_i$. Then $\mathcal{L}$ can be written as below,

$$\mathcal{L} = \sum_{i=1}^{r} D_i \mathfrak{L}_i. \tag{3.5}$$

Some times it is easier to use expression (3.5) for $\mathcal{L}$ to prove theorems in this paper.

For a fixed $i \in \{1, \ldots, n\}$, let λ_i^k be the kth Neumann eigenvalue of the operator $-\mathcal{L}_i$ as in (3.3) ($\lambda_i^1 = 0$, $\lambda_i^k > 0$ for $k > 1$, and $\lambda_i^k \to \infty$ as $k \to \infty$) and e_i^k be the corresponding normalized eigenfunction:

$$\nabla \cdot \left(A_i(\omega) \nabla e_i^k(\omega) \right) = -\lambda_i^k e_i^k(\omega), \quad \omega \in \Omega$$
$$\nabla e_i^k(\xi) \cdot \mathbf{n} = 0, \qquad \xi \in \partial\Omega \tag{3.6}$$

Also for each $i = 1, \ldots, r$, let $\boldsymbol{\lambda}_i^k$ be the kth Neumann eigenvalue of $-\mathbf{L}_i$. Note that

$$\Lambda_k = \sum_{i=1}^{r} \boldsymbol{\lambda}_i^k D_i, \quad \text{where} \quad \Lambda_k = \operatorname{diag}\left(\lambda_1^k, \ldots, \lambda_n^k \right). \tag{3.7}$$

For each $k \in \{1, 2, \ldots\}$, let E_i^k be the subspace spanned by the first kth eigenfunctions:

$$E_i^k = \langle e_i^1, \ldots, e_i^k \rangle.$$

Now define the map $\Pi_{k,i}$ on $L^2(\Omega)$ as follows:

$$\Pi_{k,i}(v) = v - \pi_{k,i}(v),$$

where $\pi_{k,i}$ is the orthogonal projection map onto E_i^{k-1}, and we define $E_i^0 = 0$. Namely for any $v = \sum_{j=1}^{\infty} (v, e_i^j) e_i^j$,

$$\pi_{k,i}(v) = \sum_{j=1}^{k-1} (v, e_i^j) e_i^j \quad \text{and} \quad \Pi_{k,i}(v) = \sum_{j=k}^{\infty} (v, e_i^j) e_i^j, \quad \text{for } k > 1,$$
$$\pi_{1,i}(v) = 0, \quad \text{and} \quad \Pi_{1,i}(v) = v; \tag{3.8}$$

where $(x, y) := \int x^T y$. Note that for any $i = 1, \ldots, n$,

$$\Pi_{2,i}(v) = v - \frac{1}{|\Omega|} \int_{\Omega} v. \tag{3.9}$$

For any $v = (v_1, \ldots, v_n)$, define Π_k as follows:

$$\Pi_k(v) = v - \pi_k(v) \quad \text{where} \quad \pi_k(v) = \left(\pi_{k,1}(v_1), \ldots, \pi_{k,n}(v_n) \right)^T.$$

Observe that $\pi_k(v)$ is the orthogonal projection map onto $E_1^{k-1} \times \cdots \times E_n^{k-1}$.

Definition 1 By a solution of the PDE

$$\frac{\partial u}{\partial t}(\omega, t) = F(u(\omega, t), t) + \mathcal{L}u(\omega, t),$$
$$\nabla u_i \cdot \mathbf{n}(\xi, t) = 0 \quad \forall \xi \in \partial\Omega, \quad \forall t \in [0, \infty)$$

on an interval $[0, T)$, where $0 < T \leq \infty$, we mean a function $u = (u_1, \ldots, u_n)^T$, with $u \colon \bar{\Omega} \times [0, T) \to V$, such that:

1. for each $\omega \in \bar{\Omega}$, $u(\omega, \cdot)$ is continuously differentiable;
2. for each $t \in [0, T)$, $u(\cdot, t)$ is in $\mathbf{Y}$, where $\mathbf{Y}$ is defined as the following set:

$$\left\{ v = (v_1, \ldots, v_n)^T : \bar{\Omega} \to V \mid v_i \in C^2_{\mathbb{R}}\left(\bar{\Omega}\right), \quad \frac{\partial v_i}{\partial \mathbf{n}}(\xi) = 0, \ \forall \xi \in \partial\Omega \ \ \forall i \right\},$$

   where $C^2_{\mathbb{R}}\left(\bar{\Omega}\right)$ is the set of twice continuously differentiable functions $\bar{\Omega} \to \mathbb{R}$.
3. for each $\omega \in \bar{\Omega}$, and each $t \in [0, T)$, u satisfies the above PDE.

Theorems on existence and uniqueness of solutions for PDEs such as (3.1)–(3.2) can be found in standard references, e.g. [5, 22].

For any invertible matrix Q, and any $1 \le p \le \infty$, and continuous $u \colon \Omega \to \mathbb{R}^n$, we denote the weighted $L_{p,Q}$ norm, $\|u\|_{p,Q} = \|Qu\|_p$, where $(Qu)(\omega) = Qu(\omega)$ and $\|\cdot\|_p$ indicates the norm in $L^p(\Omega, \mathbb{R}^n)$.

Definition 2 Let $(X, \|\cdot\|_X)$ be a finite dimensional normed vector space over $\mathbb{R}$ or $\mathbb{C}$. The space $\mathcal{L}(X, X)$ of linear transformations $M \colon X \to X$ is also a normed vector space with the induced operator norm

$$\|M\|_{X\to X} = \sup_{\|x\|_X=1} \|Mx\|_X.$$

The logarithmic norm $\mu_X(\cdot)$ induced by $\|\cdot\|_X$ is defined as the directional derivative of the matrix norm, that is,

$$\mu_X(M) = \lim_{h\to 0^+} \frac{1}{h}\left(\|I + hM\|_{X\to X} - 1\right),$$

where I is the identity operator on X.

In [1], we proved the following lemma:

Lemma 1 *Consider the PDE system (3.1)–(3.2), with $\mathcal{L} = D\Delta$, where $D = diag(d_1, \ldots, d_n)$. In addition suppose Assumption 1 holds. For some $1 \le p \le \infty$, and a positive diagonal matrix Q, let*

$$\mu := \sup_{(x,t)\in V\times[0,\infty)} \mu_{p,Q}(J_F(x,t)).$$

(We are using $\mu_{p,Q}$ to denote the logarithmic norm associated to the norm $\|Qv\|_p$ in $\mathbb{R}^n$.) Then for any two solutions u and v of (3.1)–(3.2), we have

$$\|u(\cdot,t) - v(\cdot,t)\|_{p,Q} \le e^{\mu t}\|u(\cdot,0) - v(\cdot,0)\|_{p,Q}.$$

The first part of the following theorem is a generalization of Lemma 1 to non-diagonal P for the special case of $p = 2$. The second part of the theorem is a generalization of Theorem 1 from [3] to spatially-varying diffusion.

Theorem 1 *Consider the reaction-diffusion system (3.1)–(3.2) and suppose Assumption 1 holds. For $k = 1, 2$, let*

$$\mu_k := \sup_{(x,t)\in V\times[0,\infty)} \mu_{2,P}(J_F(x,t) - \Lambda_k),$$

for a positive symmetric matrix P such that for any $i = 1, \ldots, r$:

$$P^2 D_i + D_i P^2 \; > \; 0. \tag{3.10}$$

Then for any two solutions, namely u and v, of (3.1)–(3.2), we have:

$$\|u(\cdot,t) - v(\cdot,t)\|_{2,P} \leq e^{\mu_1 t}\|u(\cdot,0) - v(\cdot,0)\|_{2,P}. \tag{3.11}$$

In addition

$$\|\Pi_2(u(\cdot,t))\|_{2,P} \; \leq \; e^{\mu_2 t}\|\Pi_2(u(\cdot,0))\|_{2,P}. \tag{3.12}$$

Before proving the main theorem of this section, Theorem 1, we first prove the following:

Lemma 2 *Suppose that P is a positive definite, symmetric matrix and M is an arbitrary matrix.*

1. *If $\mu_{2,P}(M) = \mu$, then $QM + M^T Q \leq 2\mu Q$, where $Q = P^2$.*
2. *If for some $Q = Q^T > 0$, $QM + M^T Q \leq 2\mu Q$, then there exists $P = P^T > 0$ such that $P^2 = Q$ and $\mu_{2,P}(M) \leq \mu$.*

Proof First suppose $\mu_{2,P}(M) = \mu$. By definition of μ:

$$\frac{1}{2}\left(PMP^{-1} + \left(PMP^{-1}\right)^T\right) \leq \mu I.$$

Since P is symmetric, so is P^{-1}, so

$$PMP^{-1} + P^{-1}M^T P \leq 2\mu I.$$

Now multiplying the last inequality by P on the right and the left, we get:

$$P^2 M + M^T P^2 \leq 2\mu P^2.$$

This proves 1. Now assume that for some $Q = Q^T > 0$, $QM + M^T Q \leq 2\mu Q$. Since $Q > 0$, there exists $P > 0$ such that $P^T P = Q$; moreover, because Q is symmetric, so is P. Hence we have:

$$P^2 M + M^T P^2 \leq 2\mu P^2.$$

Multiplying the last inequality by P^{-1} from right and from left, we conclude 2. □

Remark 1 Observe that for $Q > 0$,

1.
$$QM + M^T Q \leq \mu Q \quad \Rightarrow \quad QM + M^T Q \ \leq \ \beta I,$$

where $\beta = \mu\lambda$ and λ is the smallest eigenvalue of Q.

2.
$$QM + M^T Q \ \leq \ \beta I \quad \Rightarrow \quad QM + M^T Q \ \leq \ \gamma Q,$$

where $\gamma = \dfrac{\beta}{\lambda'}$ and λ' is the largest eigenvalue of Q.

We now recall a result following from the Poincaré principle as in [13], which gives a variational characterization of the eigenvalues of an elliptic operator.

Lemma 3 *Consider an elliptic operator as in (3.3) and let $v = v(\omega)$ be a function not identically zero in $L^2(\Omega)$ with derivatives $\dfrac{\partial v}{\partial \omega_j} \in L^2(\Omega)$ that satisfies the Neumann boundary condition, $\nabla v(\omega) \cdot \mathbf{n}(\omega) = 0$, and for any $j \in \{1, \ldots, k-1\}$, $\int_\Omega v e_i^j = 0$. Then the following inequality holds, for any $k \geq 1$:*

$$\int\limits_\Omega \nabla v \cdot (A_i(\omega)\nabla v)\, d\omega \geq \lambda_i^k \int\limits_\Omega v^2\, d\omega. \tag{3.13}$$

Lemma 4 *Suppose $u \in L^2(\Omega)$ satisfies the Neumann boundary conditions. For any $k \in \{1, 2, \ldots\}$,*

$$(\Pi_k(u), \mathcal{L}\Pi_k(u)) \ \leq \ -(\Pi_k(u), \Lambda_k \Pi_k(u)). \tag{3.14}$$

In addition for $k = 1, 2$ and any $n \times n$ symmetric matrix Q with the following property:

$$QD_i + D_i Q \ > \ 0 \qquad i = 1, \ldots, r, \tag{3.15}$$

we have:

$$(\Pi_k(u), Q\mathcal{L}\Pi_k(u)) \ \leq \ -(\Pi_k(u), Q\Lambda_k \Pi_k(u)). \tag{3.16}$$

Proof Note that by (3.6), for any $\xi \in \partial\Omega$,

$$\nabla \Pi_{k,i}(u_i(\xi)) \cdot \mathbf{n} = \sum_{j=k}^{\infty} (u_i, e_i^j) \nabla e_i^j(\xi) \cdot \mathbf{n} = 0.$$

Also by the definition of $\Pi_{k,i}$, for any $j = 1, \ldots, k-1$,

$$\int_{\Omega} \Pi_{k,i}(u_i)e_i^j \, d\omega \;=\; 0.$$

Then by this last equality, Green's identity and Lemma 3 we get:

$$\begin{aligned}
&(\Pi_k(u), \mathcal{L}\Pi_k(u)) \\
&= \int_{\Omega} \Pi_k(u)^T \left(\nabla \cdot \left(A_1(\omega)\nabla \Pi_{k,1}(u_1)\right), \ldots, \nabla \cdot \left(A_n(\omega)\nabla \Pi_{k,n}(u_n)\right)\right)^T d\omega \\
&= \sum_{i=1}^{n} \int_{\Omega} \Pi_{k,i}(u_i)\nabla \cdot \left(A_i(\omega)\nabla \Pi_{k,i}(u_i)\right) \, d\omega \\
&= \sum_{i=1}^{n} \int_{\partial\Omega} \Pi_{k,i}(u_i) A_i(\omega)\nabla \Pi_{k,i}(u_i) \cdot \mathbf{n} \, dS \\
&\quad - \sum_{i=1}^{n} \int_{\Omega} \nabla \Pi_{k,i}(u_i)^T A_i(\omega)\nabla \Pi_{k,i}(u_i) \, d\omega \\
&\leq - \sum_{i=1}^{n} \lambda_i^k \int_{\Omega} \Pi_{k,i}^2(u_i) \, d\omega \\
&= -\left(\Pi_k(u), \Lambda_k \Pi_k(u)\right).
\end{aligned}$$

Since for each $i = 1, \ldots, r$, $QD_i + D_i Q > 0$, there exists positive definite symmetric matrix M_i, such that $QD_i + D_i Q = 2M_i^T M_i$. Note that

$$\begin{aligned}
2\left(\Pi_k(u), QD_i\mathfrak{L}_i\Pi_k(u)\right) = &\left(\Pi_k(u), (QD_i + D_i Q)\mathfrak{L}_i\Pi_k(u)\right) \\
&+ \left(\Pi_k(u), (QD_i - D_i Q)\mathfrak{L}_i\Pi_k(u)\right).
\end{aligned}$$

A simple calculation shows that $(\Pi_k(u), (QD_i - D_i Q)\mathfrak{L}_i\Pi_k(u)) = 0$:

Let $Y = QD_i$. Then since Q and D_i are symmetric, $Y^T = D_i Q$. Also let $x = \Pi_k(u)$ and $y = Yx = QD_i\Pi_k(u)$. By the definition of $\mathfrak{L}_i$, $Y\mathfrak{L}_i = \mathfrak{L}_i Y$, hence we need to show:

$$(x, \mathfrak{L}_i y) \;=\; (y, \mathfrak{L}_i x).$$

By the definition of $\mathfrak{L}_i$, it suffices to show that for any $j = 1, \ldots, n$:

$$(x_j, \mathbf{L}_i y_j) \;=\; (y_j, \mathbf{L}_i x_j).$$

This last equality holds by the definition of $\mathbf{L}_i$, the Neumann boundary condition, and Green's identity. Therefore, using (3.14), for $k = 1, 2$, we get

$$
\begin{aligned}
(\Pi_k(u), QD_i\mathfrak{L}_i\Pi_k(u)) &= \frac{1}{2}(\Pi_k(u), (QD_i + D_iQ)\mathfrak{L}_i\Pi_k(u)) \\
&= \left(\Pi_k(u), M_i^T M_i\mathfrak{L}_i\Pi_k(u)\right) \\
&= (M_i\Pi_k(u), M_i\mathfrak{L}_i\Pi_k(u)) \\
&= (M_i\Pi_k(u), \mathfrak{L}_i M_i\Pi_k(u)) \\
&= (\Pi_k(M_iu), \mathfrak{L}_i\Pi_k(M_iu)) \\
&\leq -\boldsymbol{\lambda}_i^k\,(\Pi_k(M_iu), \Pi_k(M_iu)) \\
&= -\boldsymbol{\lambda}_i^k\,(\Pi_k(u), QD_i\Pi_k(u))\,. \qquad (3.17)
\end{aligned}
$$

Note that by the definition of $\mathfrak{L}_i$, $M_i\mathfrak{L}_i = \mathfrak{L}_iM_i$. By (3.8) and (3.9), for any $i, j = 1, \ldots, n$,

$$\Pi_{k,i} = \Pi_{k,j} \quad \text{for} \quad k = 1, 2.$$

Therefore $M_i\Pi_k(u) = \Pi_k(M_iu)$ and for any l, $\Pi_{k,l}(M_iu)$ is orthogonal to e_i^1. Hence we can apply the Poincaré principle. Now using (3.5) and (3.17), we get:

$$
\begin{aligned}
(\Pi_k(u), Q\mathcal{L}\Pi_k(u)) &= \sum_{i=1}^{r}(\Pi_k(u), QD_i\mathfrak{L}_i\Pi_k(u)) \\
&\leq -\sum_{i=1}^{r}\boldsymbol{\lambda}_i^k\,(\Pi_k(u), QD_i\Pi_k(u)) \\
&= -\,(\Pi_k(u), Q\Lambda_k\Pi_k(u))\,. \qquad (3.18)
\end{aligned}
$$

The last equality holds by Eq. (3.7). □

Lemma 5 *Suppose $u \in L^2(\Omega)$ satisfies the Neumann boundary conditions. For any $k \in \{1, 2, \ldots\}$,*

$$\Pi_k\,(\mathcal{L}u) = \mathcal{L}\Pi_k(u).$$

Proof By the definition of Π_k and $\mathcal{L}$, it is enough to show that for a fixed $i (i = 1, \ldots, n)$,

$$\Pi_{k,i}\,(\mathcal{L}_iu_i) = \mathcal{L}_i\Pi_{k,i}(u_i). \qquad (3.19)$$

Using the fact that $\mathcal{L}_ie_i^j = -\lambda_i^je_i^j$, the right hand side of (3.19) becomes:

$$\mathcal{L}_i\Pi_{k,i}(u_i) = \mathcal{L}_i\sum_{i=k}^{\infty}(u_i, e_i^j)e_i^j = \sum_{i=k}^{\infty}(u_i, e_i^j)\mathcal{L}_ie_i^j = -\sum_{i=k}^{\infty}(u_i, e_i^j)\lambda_i^je_i^j;$$

and using the orthogonality of the e_i^j's, the left hand side of (3.19) becomes:

$$\begin{aligned}
\Pi_{k,i}\,(\mathcal{L}_i u_i) &= \sum_{j=k}^{\infty}\left(\mathcal{L}_i u_i, e_i^j\right) e_i^j = \sum_{j=k}^{\infty}\left(\mathcal{L}_i \sum_{l=1}^{\infty}(u_i, e_i^l)e_i^l\ ,\ e_i^j\right)e_i^j \\
&= \sum_{j=k}^{\infty}\left(\sum_{l=1}^{\infty}(u_i, e_i^l)\mathcal{L}_i e_i^l\ ,\ e_i^j\right)e_i^j \\
&= -\sum_{j=k}^{\infty}\left(\sum_{l=1}^{\infty}(u_i, e_i^l)\lambda_i^l e_i^l\ ,\ e_i^j\right)e_i^j \\
&= -\sum_{j=k}^{\infty}(u_i, e_i^j)\lambda_i^j e_i^j .
\end{aligned}$$

Hence (3.19) holds. □

Lemma 6 *Let $w = u - x$, where u is a solution of* (3.1)–(3.2) *and $x = \pi_2(u)$ or $x = v$ is another solution of* (3.1)–(3.2). *Note that for $x = v$, $w = \Pi_1(u - v)$ and for $x = \pi_2(u)$, $w = \Pi_2(u)$. For a positive, symmetric matrix Q, let*

$$\Phi(w) \ := \ \frac{1}{2}(w, Qw).$$

Then

$$\frac{d\Phi}{dt}(w) = (w, Q(F(u,t) - F(x,t))) + (w, Q\mathcal{L}w)\,. \tag{3.20}$$

Proof For $x = v$,

$$\begin{aligned}
\frac{d\Phi}{dt}(w) &= (u - v, Q\tfrac{d}{dt}(u - v)) \\
&= (w, Q(F(u,t) - F(v,t))) \ + \ (w, Q\mathcal{L}(u - v)) \\
&= (w, Q(F(u,t) - F(x,t))) + (w, Q\mathcal{L}w)\,.
\end{aligned}$$

For $x = \pi_2(u)$, i.e. $w = \Pi_2(u)$,

$$\begin{aligned}
\frac{d\Phi}{dt}(w) &= (\Pi_2(u), Q\tfrac{d}{dt}(\Pi_2(u))) \\
&= (\Pi_2(u), Q\Pi_2(F(u,t))) \ + \ (w, Q\Pi_2(\mathcal{L}u)) \\
&= (\Pi_2(u), Q\Pi_2(F(u,t))) \ + \ (w, Q\mathcal{L}\Pi_2(u)) \quad \text{by Lemma 5} \\
&= (\Pi_2(u), Q(F(u,t) - \pi_2(F(u,t)))) \ + \ (w, Q\mathcal{L}w) \\
&= (\Pi_2(u), Q(F(u,t) - F(\pi_2(u),t))) \ + \ (w, Q\mathcal{L}w) \\
&\quad + \ (\Pi_2(u), Q(\pi_2(F(u,t)) - F(\pi_2(u),t))) \\
&= (w, Q(F(u,t) - F(x,t))) + (w, Q\mathcal{L}w)\,.
\end{aligned}$$

Note that the last equality holds because $Q(\pi_2(F(u,t)) - F(\pi_2(u),t))$ is independent of ω and $\int_\Omega \Pi_{2,i}(u) = 0$. □

Now we are ready to prove Theorem 1.

Proof of Theorem 1

Proof By Lemma 2,

$$Q(J_F - \Lambda_k) + (J_F - \Lambda_k)^T Q \leq 2\mu_k Q, \tag{3.21}$$

where $Q = P^2$. Define w and $\Phi(w)$ as in Lemma 6 for $Q = P^2$. Since $\Phi(w) = \frac{1}{2}\|Pw\|_2^2$, to prove (3.11) and (3.12), it's enough to show that for $k = 1, 2$

$$\frac{d}{dt}\Phi(w) \leq 2\mu_k \Phi(w).$$

Note that by Lemma 4, and the fact that $w = \Pi_1(u - v)$ or $w = \Pi_2(u)$, the second term of the right hand side of (3.20), $\frac{d}{dt}\Phi(w)$, satisfies:

$$(w, Q\mathcal{L}w) \leq -(w, Q\Lambda_k w). \tag{3.22}$$

Next, by the Mean Value Theorem for integrals, and using (3.21), we rewrite the first term of the right hand side of (3.20) as follows:

$$\begin{aligned}(w, Q(F(u,t) - F(x,t))) &= \int_\Omega w^T(\omega,t) Q(F(u(\omega,t),t) - F(x,t))\, d\omega \\ &= \int_\Omega w^T(\omega,t) Q \int_0^1 J_F(x + sw(\omega,t),t) \cdot w(\omega,t)\, ds\, d\omega \\ &= \int_0^1 \int_\Omega w^T(\omega,t) Q J_F(x + sw(\omega,t),t) \cdot w(\omega,t)\, d\omega\, ds.\end{aligned}$$

This last equality together with (3.22) imply:

$$\begin{aligned}&(w, Q(F(u,t) - F(x,t))) + (w, Q\mathcal{L}w) \\ &\leq \int_0^1 \int_\Omega w^T(\omega,t) Q\big(J_F(x + sw(\omega,t),t) - \Lambda_k\big) \\ &\quad \cdot w(\omega,t)\, d\omega\, ds \\ &\leq \frac{2\mu_k}{2} \int_0^1 ds \int_\Omega w^T Q w\, d\omega\end{aligned}$$

$$= \frac{2\mu_k}{2} \int_{\Omega} w^T Q w \, d\omega$$
$$= 2\mu_k \Phi(w).$$

Therefore

$$\frac{d\Phi}{dt}(w) \le 2\mu_k \Phi(w).$$

This last inequality implies (3.11) and (3.12) for $k = 1$ and $k = 2$ respectively. □

Corollary 1 *In* Theorem 1*, if* $\mu_1 < 0$*, then* (3.1)–(3.2) *is contracting, meaning that solutions converge (exponentially) to each other, as* $t \to +\infty$ *in the weighted* $L_{2,P}$ *norm:*

$$\|u(\cdot,t) - v(\cdot,t)\|_{2,P} \to 0 \quad as t \to \infty.$$

Corollary 2 *In* Theorem 1*, if* $\mu_2 < 0$*, then solutions converge (exponentially) to uniform solutions, as* $t \to +\infty$ *in the weighted* $L_{2,P}$ *norm:*

$$\|\Pi_2(u(\cdot,t))\|_{2,P} \to 0 \quad as\ t \to \infty.$$

Note that (3.16) doesn't necessarily hold for any $k > 2$, since for $k > 2$, the $\Pi_{k,i}$'s could be different for different i's. In the following lemma we provide a condition for which (3.16) holds for any k.

Lemma 7 *Assume* $P\mathcal{L} = \mathcal{L}P$*, where* P *is a positive, symmetric* $n \times n$ *matrix and* $P^2 = Q$*. Then for any* $k = 1, 2, \ldots$

$$(\Pi_k(u), Q\mathcal{L}\Pi_k(u)) \le -(\Pi_k(u), Q\Lambda_k\Pi_k(u)).$$

Proof The proof is analogous to the proof of (3.16), using the fact that $P\mathcal{L} = \mathcal{L}P$ implies that P is diagonal (if all $\mathcal{L}_i$'s are different) or block diagonal (for equal Laplacian operators). □

Remark 2 Note that Theorem 1 is valid if $P\mathcal{L} = \mathcal{L}P$ is assumed instead of (3.15), because (3.16) holds by Lemma 7 and this is all that is needed in the proof. In the following theorem we use this condition to generalize the result of Theorem 1 for any arbitrary k but restricted to linear systems. We omit the proof, which is analogous.

Theorem 2 *Consider the reaction-diffusion system* (3.1)-(3.2) *and suppose Assumption 1 holds. In addition assume that* F *is a linear function. For* $k \in \{1, 2, \ldots\}$*, let*

$$\mu_k := \sup_{(x,t) \in V \times [0,\infty)} \mu_{2,P}(J_F(x,t) - \Lambda_k),$$

for a positive symmetric matrix P *such that* $P\mathcal{L} = \mathcal{L}P$*. Then for any two solutions, namely* u *and* v*, of* (3.1)–(3.2)*, we have:*

$$\|\Pi_k\,(u(\cdot,t)-v(\cdot,t))\,\|_{2,P}\le e^{\mu_k t}\|\Pi_k\,(u(\cdot,0)-v(\cdot,0))\,\|_{2,P}. \tag{3.23}$$

Example 1 In [1] we studied the following system:

$$\begin{aligned} x_t &= z-\delta x+k_1 y-k_2(S_Y-y)x+d_1\Delta x\\ y_t &= -k_1 y+k_2(S_Y-y)x+d_2\Delta y, \end{aligned}$$

where $(x(t), y(t)) \in V = [0,\infty)\times[0,S_Y]$ for all $t\ge 0$ (V is convex), and S_Y, k_1, k_2, δ, d_1, and d_2 are arbitrary positive constants.

This two-dimensional system is a prototype for a large class of models of enzymatic cell signaling as well as transcriptional components. Generalizations to systems of higher dimensions, representing networks of such systems, may be studied as well [19].

In [19], it has been shown that for $p=1$, there exists a positive, diagonal matrix Q, independent of d_1 and d_2, such that for all $(x,y)\in V$, $\mu_{1,Q}(J_F(x,y))<0$; and then by Lemma 1 one concludes that the system is contractive.

Specifically, [1] showed that for any positive, diagonal matrix Q and any $p>1$, there exists $(x,y)\in V$ such that $\mu_{p,Q}(J_F(x,y))\ge 0$, where

$$F=(z-\delta x+k_1 y-k_2(S_Y-y)x,\,-k_1 y+k_2(S_Y-y)x)^T,$$

and

$$J_F=\begin{pmatrix}-\delta-a & b\\ a & -b\end{pmatrix},$$

with $a=k_2(S_Y-y)\in[0,k_2S_Y]$ and $b=k_1+k_2x\in[k_1,\infty)$.

Now we show that there exists some positive, symmetric (but non-diagonal) matrix P such that for all $(x,y)\in V$, $\mu_{2,P}J_F(x,y)<0$ and $P^2D+DP^2>0$, where $D=\mathrm{diag}(d_1,d_2)$. Then by Theorem 1 (for $r=1$ and $\mathbf{L}_i u_i=\Delta u_i$), and Corollary 1, one can conclude that the system is contractive.

Claim *Let* $Q=\begin{bmatrix}1&1\\1&q\end{bmatrix}$, *where* $q>\max\left\{1+\frac{\delta}{4k_1},\left(\frac{1}{2\sqrt{d}}+\frac{\sqrt{d}}{2}\right)^2\right\}$, *and* $d=\frac{d_1}{d_2}$. *Then* $QJ_F+(QJ_F)^T<0$ *and* $QD+DQ>0$.

Note that Q is symmetric and positive (because $q>1$).
Proof of Claim We first compute QJ_F:

$$\begin{bmatrix}1&1\\1&q\end{bmatrix}\begin{bmatrix}-\delta-a & b\\ a & -b\end{bmatrix}=\begin{bmatrix}-\delta & 0\\ -\delta+(q-1)a & -b(q-1)\end{bmatrix}.$$

So

$$QJ_F+(J_FQ)^T=\begin{bmatrix}-2\delta & -\delta+(q-1)a\\ -\delta+(q-1)a & -2b(q-1)\end{bmatrix}.$$

To show $QJ_F + J_F^T Q < 0$, we show that $\det\left(QJ_F(x, y) + J_F^T(x, y)Q\right) > 0$ for all $(x, y) \in V$:

$$\det\left(QJ_F + J_F^T Q\right) = 4\delta b(q-1) - (-\delta + (q-1)a)^2 .$$

Note that for any $q > 1$, $f(a) := (-\delta + (q-1)a)^2 \le \delta^2$ on $[0, k_2 S_Y]$, and $g(b) := 4\delta b(q-1) \ge 4\delta k_1(q-1)$ on $[k_1, \infty]$. So to have $\det > 0$, it's enough to have $4\delta k_1(q-1) - \delta^2 > 0$, i.e. $q - 1 > \dfrac{\delta^2}{4\delta k_1}$, i.e. $q > 1 + \dfrac{\delta}{4k_1}$. Now we compute $QD + DQ$:

$$QD + DQ = \begin{bmatrix} 2d_1 & d_1 + d_2 \\ d_1 + d_2 & 2qd_2 \end{bmatrix}.$$

$QD + DQ > 0$ if and only if $\det(QD + DQ) > 0$, i.e. $4d_1d_2q - (d_1 + d_2)^2 > 0$, i.e. $q > \left(\dfrac{1}{2\sqrt{d}} + \dfrac{\sqrt{d}}{2}\right)^2$, where $d = \dfrac{d_1}{d_2}$. □

Now by Remark 1 and Lemma 2, for $P = \sqrt{Q}$, $\mu_{2,P}(J_F(x, y)) < 0$, for all $(x, y) \in V$.

Example 2 We now provide an example of a class of reaction-diffusion systems $x_t = F(x) + D\Delta x$, with $x \in V$ (V convex), which satisfy the following conditions:

1. For some positive definite, diagonal matrix Q, $\sup\limits_{x \in V} \mu_{1,Q}(J_F(x)) < 0$ (and hence by Lemma 1, these systems are contractive).
2. For any positive definite, symmetric (not necessarily diagonal) matrix P, $\sup_{x \in V} \mu_{2,P}(J_F(x)) \not< 0$.

Consider two variable systems of the following type

$$x_t = -f_1(x) + g_1(y) + d_1\Delta x \tag{3.24}$$

$$y_t = f_2(x) - g_2(y) + d_2\Delta y, \tag{3.25}$$

where d_1, d_2 are positive constants and $(x, y) \in V = [0, \infty) \times [0, \infty)$. The functions f_i and g_i take non-negative values. Systems of this form model a case where x decays according to f_1, y decays according to g_2, and there is a positive feedback from y to x (g_1) and a positive feedback from x to y (f_2).

Lemma 8 *In system* (3.24)–(3.25)*, let J be the Jacobian matrix of*

$$(-f_1(x) + g_1(y), f_2(x) - g_2(y))^T .$$

In addition, assume that the following conditions hold for some $\lambda > 0$, and $\mu > 0$ and all $(x, y) \in V$:

1. $-f_1'(x) + \lambda|f_2'(x)| < -\mu < 0$;
2. $-g_2'(y) + \dfrac{1}{\lambda}|g_1'(y)| < -\mu < 0$;
3. *for any* $p_0 \in \mathbb{R}$

$$\lim_{y\to\infty} \frac{\left(g_1'(y) - p_0 g_2'(y)\right)^2}{g_2'(y)} = \infty.$$

Then

1. *for every* $(x, y) \in V$*,* $\mu_{1,Q}(J(x, y)) < 0$*, where* $Q = diag(1, \lambda)$*; and*
2. *for each positive definite, symmetric matrix* P*, there exists some* $(x, y) \in V$*, such that* $\mu_{2,P}(J(x, y)) \geq 0$.

Proof The proof of $\mu_{1,Q}(J(x, y)) < 0$ is straightforward from the definition of $\mu_{1,Q}$ and conditions 1 and 2. Now we show that for any positive matrix $P = \begin{bmatrix} p_1 & p \\ p & p_2 \end{bmatrix}$, there exists some $(x_0, y_0) \in V$ such that $\mu_{2,P}(J(x_0, y_0)) \geq 0$. By Lemma 2, it's enough to show that for some $(x_0, y_0) \in V$, $PJ(x_0, y_0) + J^T(x_0, y_0)P \not< 0$. We compute:

$$\begin{aligned} PJ &= \begin{bmatrix} p_1 & p \\ p & p_2 \end{bmatrix} \begin{bmatrix} -f_1'(x) & g_1'(y) \\ f_2'(x) & -g_2'(y) \end{bmatrix} \\ &= \begin{bmatrix} -p_1 f_1'(x) + p f_2'(x) & p_1 g_1'(y) - p g_2'(y) \\ -p f_1'(x) + p_2 f_2'(x) & p g_1'(y) - p_2 g_2'(y) \end{bmatrix}. \end{aligned}$$

Therefore, $PJ + (PJ)^T$ is equal to

$$\begin{bmatrix} 2\left(-p_1 f_1'(x) + p f_2'(x)\right) & p_1 g_1'(y) - p g_2'(y) - p f_1'(x) + p_2 f_2'(x) \\ p_1 g_1'(y) - p g_2'(y) - p f_1'(x) + p_2 f_2'(x) & 2\left(p g_1'(y) - p_2 g_2'(y)\right) \end{bmatrix}.$$

(not showing x and y arguments in f_1' and f_2' for simplicity). Now fix $x_0 \in [0, \infty)$ and let

$$A \;:=\; 2\left(-p_1 f_1'(x_0) + p f_2'(x_0)\right),$$

and

$$B \;:=\; -p f_1'(x_0) + p_2 f_2'(x_0).$$

Then $\det\left(PJ + (PJ)^T\right)$ is equal to

$$2A\left(p g_1'(y) - p_2 g_2'(y)\right) - \left(p_1 g_1'(y) - p g_2'(y) + B\right)^2. \tag{3.26}$$

We will show that det < 0. Dividing both sides of (3.26) by $p_1^2 g_2'(y)$, we get:

$$\begin{aligned}\frac{\det\left(PJ+(PJ)^T\right)}{p_1^2 g_2'(y)} &= \frac{2A\left(pg_1'(y)-p_2g_2'(y)\right)}{p_1^2 g_2'(y)}\\ &\quad - \frac{\left(g_1'(y)-p_0g_2'(y)+B'\right)^2}{g_2'(y)}\\ &= A'p\frac{g_1'(y)}{g_2'(y)} - A'p_2\\ &\quad - \frac{\left(g_1'(y)-p_0g_2'(y)\right)^2}{g_2'(y)} - 2B'\frac{g_1'(y)}{g_2'(y)}\\ &\quad + 2B'p_0 - \frac{B'^2}{g_2'(y)}\end{aligned}$$

where $p_0 = \dfrac{p}{p_1}$, $A' = \dfrac{2A}{p_1^2}$, and $B' = \dfrac{B}{p_1}$.

(Note that $p_1^2 g_2'(y) > 0$ because by condition 2, $g_2' \geq \mu > 0$, and $P > 0$ implies $p_1 \neq 0$.)

By condition 2, $0 \leq \dfrac{g_1'(y)}{g_2'(y)} \leq \lambda < \infty$ for all y. Now using condition 3, we can find y large enough such that det < 0.

Since $\det\left(PJ(x_0,y_0)+(PJ(x_0,y_0))^T\right) < 0$ for some $(x_0,y_0) \in V$, the matrix $PJ+(PJ)^T$ has one positive eigenvalue. Therefore $PJ+(PJ)^T \nless 0$. □

Example 3 As a concrete example, take the following system

$$\begin{aligned}x_t &= -x + y^{2+\epsilon} + d_1\Delta x\\ y_t &= \delta x - (y^3 + y^{2+\epsilon} + dy) + d_2\Delta y,\end{aligned}$$

where $0 < \delta < 1$, $0 < \epsilon \ll 1$, d, d_1, and d_2 are positive constants and $(x,y) \in V = [0,\infty) \times [0,\infty)$.

In this example we show that, the system is contractive in a weighted L^1 norm; while for any positive, symmetric matrix P, and some $(x,y) \in V$, $\mu_{2,P} J_F(x,y) \nless 0$. To this end, we verify the conditions of Lemma 8.

For any $(x,y) \in V$, we take in Lemma 8, $\lambda = 1$, and any $\mu \in (0, \min\{d, 1-\delta\})$:

1. $-1+\delta < 0$, because $0 < \delta < 1$.
2. $-\left(3y^2 + (2+\epsilon)y^{1+\epsilon} + d\right) + (2+\epsilon)y^{1+\epsilon} = -3y^2 - d \leq -d < 0$.
3. For any $p_0 \in \mathbb{R}$,

$$\lim_{y\to\infty} \frac{\left((1-p_0)(2+\epsilon)y^{1+\epsilon} - p_0\left(3y^2+d\right)\right)^2}{3y^2 + (2+\epsilon)y^{1+\epsilon} + d} = \infty$$

So the conditions in Lemma 8 are verified. □

3.3 Spatial Uniformity in Diffusively-Coupled Systems of ODEs

We next consider a compartmental ODE model where each compartment represents a spatial domain interconnected with the other compartments over an undirected graph:

$$\dot{u}(t) = \tilde{F}(u(t)) - \mathcal{L}u(t). \tag{3.27}$$

Recall that if $A = (a_{ij})$ is an $m \times n$ matrix and $B = (b_{ij})$ is a $p \times q$ matrix, then the Kronecker product, denoted by $A \otimes B$, is the $mp \times nq$ block matrix defined as follows:

$$A \otimes B \ := \begin{bmatrix} a_{11}B & \dots & a_{1n}B \\ \vdots & \ddots & \vdots \\ a_{m1}B & \dots & a_{mn}B \end{bmatrix},$$

where $a_{ij}B$ denote the following $p \times q$ matrix:

$$a_{ij}B \ := \begin{bmatrix} a_{ij}b_{11} & \dots & a_{ij}b_{1q} \\ \vdots & \ddots & \vdots \\ a_{ij}b_{p1} & \dots & a_{ij}b_{pq} \end{bmatrix}.$$

The following are some properties of Kronecker product:

1. $(A \otimes B)(C \otimes D) = (AC) \otimes (BD)$;
2. $(A \otimes B)^T = A^T \otimes B^T$.
3. Suppose that A and B are square matrices of size n and m respectively. Let $\lambda_1, \dots, \lambda_n$ be the eigenvalues of A and $\mu_1, \dots, \mu_m$ be those of B (listed according to multiplicity). Then the eigenvalues of $A \otimes B$ are $\lambda_i \mu_j$ for $i = 1, \dots, n$, and $j = 1, \dots, m$.

Assumption 2 In (3.27), we assume:

- For a fixed convex subset of $\mathbb{R}^n$, say V, $\tilde{F}\colon V^N \to \mathbb{R}^{nN}$ is a function of the form:

$$\tilde{F}(u) = \left(F(u^1)^T, \dots, F(u^N)^T\right)^T,$$

  where $u = \left((u^1)^T, \dots, (u^N)^T\right)^T$, with $u^i \in V$ for each i, and $F\colon V \to \mathbb{R}^n$ is a (globally) Lipschitz function.
- For any $u \in V^N$ we define $\|u\|_{p,Q}$ as follows:

$$\|u\|_{p,Q} = \left\| \left(\|Qu^1\|_p, \dots, \|Qu^N\|_p\right)^T \right\|_p,$$

  where Q is a symmetric and positive definite matrix and $1 \leq p \leq \infty$.

With a slight abuse of notation, we use the same symbol for a norm in $\mathbb{R}^n$:

$$\|x\|_{p,Q} := \|Qx\|_p.$$

- $u\colon [0,\infty) \to V^N$ is a continuously differentiable function.
- $$\mathcal{L} = \sum_{i=1}^{n} L_i \otimes E_i,$$

  where for any $i = 1,\dots,n$, $L_i \in \mathbb{R}^{N\times N}$ is a symmetric positive semidefinite matrix and $L\mathbf{1}_N = 0$, where $\mathbf{1}_N = (1,\dots,1)^T \in \mathbf{R}^N$. The matrix L_i is the symmetric generalized graph Laplacian (see, e.g., [10]) that describes the interconnections among component subsystems. For any $i = 1,\dots,n$, $E_i = e_i e_i^T \in \mathbb{R}^{n\times n}$ is the product of the ith standard basis vector e_i multiplied by its transpose.

Similar to the PDE case, we assume that there exists $r \le n$ distinct matrices, $\mathbf{L}_1,\dots,\mathbf{L}_r$ such that

$$\begin{aligned}&\operatorname{diag}\left(L_1,\dots,L_{n_1},\dots,L_{n-n_r+1},\dots,L_n\right)\\ &\quad= \operatorname{diag}\left(d_{11},\dots,d_{1n_1},\dots,d_{r1},\dots,d_{rn_r}\right)\operatorname{diag}\left(\mathbf{L}_1,\dots,\mathbf{L}_1,\dots,\mathbf{L}_r,\dots,\mathbf{L}_r\right),\end{aligned}$$

where $n_1+\cdots+n_r = n$. For each $i = 1,\dots,r$, let D_i be an $n\times n$ diagonal matrix with entries $[D_i]_{n_{i-1}+j,n_{i-1}+j} = d_{ij}$, for $j = 1,\dots,n_i$, $n_0 = 0$ elsewhere. Therefore we can write $\mathcal{L}$ as follows:

$$\mathcal{L} = \sum_{i=1}^{r} \mathbf{L}_i \otimes D_i \tag{3.28}$$

For a fixed $i \in \{1,\dots,n\}$, let λ_i^k be the kth eigenvalue of the matrix L_i and e_i^k be the corresponding normalized eigenvector. Also for a fixed $i \in \{1,\dots,r\}$, let $\boldsymbol{\lambda}_i^k$ be the kth eigenvalue of the matrix $\mathbf{L}_i$. Note that

$$\Lambda_k = \sum_{i=1}^{r} \boldsymbol{\lambda}_i^k D_i, \tag{3.29}$$

where $\Lambda_k = \operatorname{diag}(\lambda_1^k,\dots,\lambda_n^k)$.

For each $k \in \{1,2,\dots,N\}$, let E_i^k be the subspace spanned by the first kth eigenvectors:

$$E_i^k = \langle e_i^1,\dots,e_i^k\rangle.$$

Now let $\pi_{k,i}$ be the orthogonal projection map from $\mathbb{R}^N$ onto E_i^{k-1}. Namely for any $v = \sum_{j=1}^{N}(v\cdot e_i^j)e_i^j$,

$$\pi_{k,i}(v) \ = \ \sum_{j=1}^{k-1}(v \cdot e_i^j)e_i^j,$$

for $1 < k \leq N$ and $\pi_{1,i}(v) = 0$.

Now for $u = (u^1, \ldots, u^N)$ with $u^j \in \mathbb{R}^n$, define $\pi_k(u)$ as follows:

$$\pi_k(u) \ = \ \sum_{j=1}^{n}(\pi_{j,k}(u_j))^T \otimes e_j, \tag{3.30}$$

for $1 < k \leq N$, where $u_j := (u^1 \cdot e_j, \ldots, u^N \cdot e_j)^T$; and $\pi_1(u) = 0$.

Note that for each k and any $u, v \in \mathbb{R}^{nN}$,

$$(u - \pi_k(u))^T \, \pi_k(v) \ = \ \sum_{j=1}^{n} \left(u_j - \pi_{j,k}(u_j)\right)^T \pi_{j,k}(v_j) \ = \ 0. \tag{3.31}$$

We also can define $\pi_k(u)$ as follows:

For $i = 1, \ldots, n$, let $e^i := \sum_{j=1}^{N} e_i^j \otimes e_j$. It is straightforward to show that $e^1, \ldots, e^n$ are linearly independent and for any $i, j \in \{1, \ldots, n\}$, ${e^i}^T e^j = 0$. Hence one can extend $\left\{e^i\right\}_{1 \leq i \leq n}$ to an orthogonal basis for $\mathbb{R}^{nN}$, $\left\{e^i\right\}_{1 \leq i \leq nN}$. Then for each $k = 2, \ldots, nN$, and any $u \in \mathbf{R}^{nN}$,

$$\pi_k(u) \ = \ \sum_{j=1}^{k-1} \left(u \cdot e^j\right) e^j,$$

and $\pi_1(u) = 0$. Note that for $k = 1, \ldots, n$, this definition is compatible with (3.30).

We now state Courant-Fischer minimax theorem, from [14].

Lemma 9 *Let L be a symmetric, positive semidefinite matrix in $\mathbb{R}^{N \times N}$. Let $\lambda^1 \leq \cdots \leq \lambda^N$ be N eigenvalues with $e^1, \ldots, e^N$ corresponding normalized orthogonal eigenvectors. For any $v \in \mathbb{R}^N$, if $v^T e^j = 0$ for $1 \leq j \leq k-1$, then*

$$v^T L v \geq \lambda^k v^T v.$$

Lemma 10 *Let $w := u - x$, where u is a solution of (3.27) and $x = v$ is another solution of (3.27) or $x = \pi_2(u)$, i.e. $x = \mathbf{1}_N \otimes \left(\frac{1}{N}\sum_{j=1}^{N} u^j\right)$. For a positive, symmetric matrix Q, let*

$$\Phi(w) \ := \ \frac{1}{2} w^T \left(I_N \otimes Q\right) w.$$

Then

$$\frac{d\Phi}{dt}(w) = w^T\,(I_N \otimes Q)\,(\tilde{F}(u,t) - \tilde{F}(x,t)) - w^T\,(I_N \otimes Q)\,\mathcal{L}w. \tag{3.32}$$

Proof When $x = v$, the claim is trivial because both u and v satisfy (3.27). When $x = \pi_2(u)$, then, by orthogonality, Eq. (3.31), and the definition of π_2, we have:

$$\begin{aligned}\frac{d\Phi}{dt}(w) &= (u - \pi_2(u))^T\,(I_N \otimes Q)\,(\tilde{F}(u,t) - \pi_2(\tilde{F}(u,t))) + w^T\,(I_N \otimes Q)\,\mathcal{L}w\\ &= (u - \pi_2(u))^T\,(I_N \otimes Q)\,\tilde{F}(u,t) + w^T\,(I_N \otimes Q)\,\mathcal{L}w\\ &= (u - \pi_2(u))^T\,(I_N \otimes Q)\,(\tilde{F}(u,t) - \tilde{F}(\pi_2(u),t)) + w^T\,(I_N \otimes Q)\,\mathcal{L}w,\end{aligned}$$

The last equality holds because

$$\begin{aligned}(u - \pi_2(u))^T\,(I_N \otimes Q)\,\tilde{F}(\pi_2(u),t)) &= \sum_{j=1}^{N}(u^j - \bar{u})QF(\bar{u})\\ &= \left(\sum_{j=1}^{N} u^j - N\bar{u}\right) QF(u) \;=\; 0,\end{aligned}$$

where $\bar{u} = \frac{1}{N}\sum_{j=1}^{N} u^j$.

Theorem 3 *Consider the ODE system* (3.27) *and suppose Assumption 2 holds. For* $k = 1, 2$*, let*

$$\mu_k := \sup_{(x,t)\in V\times[0,\infty)} \mu_{2,P}(J_F(x,t) - \Lambda_k),$$

for a positive symmetric matrix P *such that for every* $i = 1, \ldots, r$*,*

$$P^2 D_i + D_i P^2 > 0.$$

Then for any two solutions, namely u *and* v*, of* (3.27)*, we have:*

$$\|(u - v)(t)\|_{2,P} \leq e^{\mu_1 t}\|(u - v)(0)\|_{2,P}. \tag{3.33}$$

In addition

$$\|(u - \pi_2(u))(t)\|_{2,P} \;\leq\; e^{\mu_2 t}\|(u - \pi_2(u))(0)\|_{2,P}. \tag{3.34}$$

Proof By Lemma 2,

$$Q(J_F - \Lambda_k) + (J_F - \Lambda_k)^T Q \leq 2\mu_k Q, \tag{3.35}$$

where $Q = P^2$. Define w and $\Phi(w)$ as in Lemma 10 for $Q = P^2$. Since $\Phi(w) = \frac{1}{2}\|Pw\|_2^2$, to prove (3.33) and (3.34), it's enough to show that for $k = 1, 2$

$$\frac{d}{dt}\Phi(w) \leq 2\mu_k \Phi(w).$$

We rewrite the second term of the right hand side of (3.32) as follows. Since $Q = P^2$ and $P^2 D_i + D_i P^2 > 0$, there exists symmetric, positive definite matrices M_i such that $QD_i + D_i Q = 2M_i^T M_i$.

$$\begin{aligned}
w^T(I_N \otimes Q)\mathcal{L}w &= w^T(I_N \otimes Q)\left(\sum_{i=1}^{r} \mathbf{L}_i \otimes D_i\right) w \\
&= w^T \left(\sum_{i=1}^{r} I_N \mathbf{L}_i \otimes QD_i\right) w \\
&= \frac{1}{2}\sum_{i=1}^{r} w^T \left(\mathbf{L}_i \otimes (QD_i + D_i Q)\right) w \\
&= \sum_{i=1}^{r} w^T \left(\mathbf{L}_i \otimes M_i^T M_i\right) w \\
&= \sum_{i=1}^{r} w^T (I_N \otimes M_i^T)\,(\mathbf{L}_i \otimes I_n)\,(I_N \otimes M_i)\, w \\
&\geq \sum_{i=1}^{r} \boldsymbol{\lambda}_i^k \left((I_N \otimes M_i)w\right)^T (I_N \otimes M_i)w \quad (\text{for } k = 1, 2) \\
&= \sum_{i=1}^{r} \boldsymbol{\lambda}_i^k w^T (I_N \otimes M_i^T M_i)w \\
&= \sum_{i=1}^{r} \boldsymbol{\lambda}_i^k w^T (I_N \otimes QD_i)w \\
&= w^T(I_N \otimes Q\Lambda_k)w \qquad [\text{by Eq. (29)}]
\end{aligned}$$

Therefore

$$-w^T(I_N \otimes Q)\mathcal{L}w \leq -w^T(I_N \otimes Q\Lambda_k)w. \tag{3.36}$$

Note that the first inequality holds for $k = 2$ by Lemma 9 and the fact that for $x = \pi_2(u)$, by definition, $w^T \mathbf{1}_{nN} = 0$ and hence $(I_N \otimes M_i)\, w\mathbf{1}_{nN} = 0$. It also holds for $k = 1$, since $\mathbf{L}_i$ and hence $\mathbf{L}_i \otimes I_n$ are positive definite, and $\boldsymbol{\lambda}_i^1 = 0$.

Now, by the Mean Value Theorem for integrals, and using (3.21), we rewrite the first term of the right hand side of (3.32) as follows:

$$w^T\,(I_N\otimes Q)\,(\tilde F(u,t)-\tilde F(x,t)) = \sum_{i=1}^{N} {w^i}^T Q(F(u^i,t)-F(x^i,t))w^i\ ds$$
$$= \sum_{i=1}^{N}\int_0^1 {w^i}^T Q J_F(x^i+sw^i,t)w^i\ ds.$$

This last equality together with (3.36) imply:

$$\begin{aligned}
&w^T\,(I_N\otimes Q)\,(\tilde F(u,t)-\tilde F(x,t)) - w^T(I_N\otimes Q)\mathcal{L}w\\
&=\sum_{i=1}^{N}\int_0^1 {w^i}^T Q\left(J_F(x^i+sw^i,t)-\Lambda_k\right)w^i\ ds\\
&\le \sum_{i=1}^{N}\frac{2\mu_k}{2}\int_0^1 ds\ {w^i}^T Q w^i\\
&=\frac{2\mu_k}{2}w^T(I_N\otimes Q)w\\
&=2\mu_k\Phi(w).
\end{aligned}$$

Therefore

$$\frac{d\Phi}{dt}(w)\ \le\ 2\mu_k\Phi(w).$$

This last inequality implies (3.33) and (3.34) for $k=1$ and $k=2$ respectively. □

Corollary 3 *In* Theorem 3*, if* $\mu_1<0$*, then* (3.27) *is contracting, meaning that solutions converge (exponentially) to each other, as* $t\to+\infty$ *in the* P*-weighted* L_2 *norm.*

Corollary 4 *In* Theorem 3*, if* $\mu_2<0$*, then solutions converge (exponentially) to uniform solutions, as* $t\to+\infty$ *in the* P*-weighted* L_2 *norm.*

3.4 LMI Tests for Guaranteeing Spatial Uniformity

The next two results are modifications of Theorems 2 and 3 in [3]. They allow us to apply check the conditions in Theorems 1 and 3 through numerical tests involving linear matrix inequalities.

Proposition 1 *If there exist constant matrices* $Z_1,\dots,Z_q$ *and* $S_l,\dots,S_m$ *such that for all* $x\in V,\ t\in[0,\infty)$*,*

$$J_F(x,t)\in conv\{Z_1,\dots,Z_q\}+cone\{S_l,\dots,S_m\}, \tag{3.37}$$

where

$$conv(Z_1, \ldots, Z_q) = \{a_1 Z_1 + \cdots a_q Z_q \mid a_i \geq 0, \sum_i a_i = 1\},$$

and

$$cone(S_1, \ldots, S_m) = \{b_1 S_1 + \cdots b_m S_m \mid b_i \geq 0\},$$

then the existence of a scalar μ *and symmetric, positive definite matrix* Q *satisfying*

$$\begin{array}{c} Q\,(Z_i - \Lambda_k) + (Z_i - \Lambda_k)^T\, Q < \mu Q,\ i = 1, \ldots, q \\ Q S_i + S_i^T\, Q \leq 0,\ i = 1, \ldots, m \end{array} \tag{3.38}$$

implies that:

$$Q(J_F(x,t) - \Lambda_k) + (J_F(x,t) - \Lambda_k)^T\, Q < \mu Q \tag{3.39}$$

for all $(x, t) \in V \times [0, \infty)$*; or equivalently*

$$\mu_k \ := \sup_{(x,t)\in V\times[0,\infty)} \mu_{2,P}(J_F(x,t) - \Lambda_k) < \frac{\mu}{2}, \tag{3.40}$$

where $P^2 = Q$.

If the image of $V \times [0, \infty)$ *under* J_F *is surjective onto* $conv\{Z_1, \ldots, Z_q\} + cone\{S_l, \ldots, S_m\}$*, then the converse is true.*

Proof First, we rewrite the first set of conditions of (3.38) as:

$$Q\left(Z_i - \Lambda_k - \frac{\mu}{2}I\right) + \left(Z_i - \Lambda_k - \frac{\mu}{2}I\right)^T Q < 0, \quad i = 1, \ldots, q \tag{3.41}$$

Defining $D = \Lambda_k + \frac{\mu}{2}I$, we can rewrite (3.41) as:

$$Q\,(Z_i - D) + (Z_i - D)^T\, Q < 0, \quad i = 1, \ldots, q. \tag{3.42}$$

An application of [3, Theorem 2] concludes the proof. Also an application of Lemma (2) implies that (3.39) and (3.40) are equivalent. □

We define a *convex box* as:

$$\text{box}\{M_0, M_1, \ldots, M_p\} = \{M_0 + \omega_1 M_1 + \ldots + \omega_p M_p \,|\, \omega_i \in [0, 1] \text{ for each } i = 1, \ldots, p\}. \tag{3.43}$$

Proposition 2 *Suppose that* $J_F(x, t)$ *is contained in a convex box:*

$$J_F(x,t) \in \text{box}\{A_0, A_1, \ldots, A_l\}\ \forall x \in V,\ t \in [0, \infty), \tag{3.44}$$

where $A_1, \dots, A_l$ *are rank-one matrices that can be written as* $A_i = B_i C_i^T$, *with* $B_i,\ C_i \in \mathbb{R}^n$. *If there exists a scalar* μ *and symmetric, positive definite matrix* $\mathcal{Q}$ *with:*

$$\mathcal{Q} = \begin{bmatrix} Q & 0 & \dots & 0 \\ 0 & p_1 & 0 & 0 \\ \vdots & \ddots & \ddots & \vdots \\ 0 & \dots & 0 & p_l \end{bmatrix} \tag{3.45}$$

$$Q \in \mathbb{R}^{n \times n}, \quad p_i \in \mathbb{R}, \quad i = 1, \dots, l,$$

satisfying:

$$\mathcal{Q}\begin{bmatrix} A_0 - \Lambda_k & B \\ C^T & -I_n \end{bmatrix} + \begin{bmatrix} A_0 - \Lambda_k & B \\ C^T & -I_n \end{bmatrix}^T \mathcal{Q} < \begin{bmatrix} \mu Q & 0 \\ 0 & 0 \end{bmatrix}, \tag{3.46}$$

with $B = [B_1 \dots B_l]$ *and* $C = [C_1 \dots C_l]$, *then the upper left (symmetric, positive definite) principal submatrix* Q *satisfies*

$$Q(J_F(x,t) - \Lambda_k) + (J_F(x,t) - \Lambda_k)^T Q < \mu Q; \tag{3.47}$$

or equivalently

$$\mu_k \ := \sup_{(x,t) \in V \times [0,\infty)} \mu_{2,P}(J_F(x,t) - \Lambda_k) < \frac{\mu}{2}, \tag{3.48}$$

where $P^2 = Q$.

If $l = 1$ *and the image of* $V \times [0, \infty)$ *under* J *is surjective onto* $\text{box}\{A_0, A_1\}$, *then the converse is true.*

Proof First, we rewrite condition (3.46) as

$$\mathcal{Q}\begin{bmatrix} A_0 - \Lambda_k - \frac{\mu}{2}I & B \\ C^T & -I_n \end{bmatrix} + \begin{bmatrix} A_0 - \Lambda_k - \frac{\mu}{2}I & B \\ C^T & -I_n \end{bmatrix}^T \mathcal{Q} < 0. \tag{3.49}$$

Defining $D = \Lambda_k + \frac{\mu}{2}I$, we can rewrite (3.41) as:

$$\mathcal{Q}\begin{bmatrix} A_0 - D & B \\ C^T & -I_n \end{bmatrix} + \begin{bmatrix} A_0 - D & B \\ C^T & -I_n \end{bmatrix}^T \mathcal{Q} < 0. \tag{3.50}$$

An application of [3, Theorem 3] concludes the proof. Also an application of Lemma (2) implies that (3.47) and (3.48) are equivalent. □

The problem of finding the smallest μ such that there exists a matrix Q as in Proposition 1 or a matrix $\mathcal{Q}$ as in Proposition 2 is quasi-convex and may be solved iteratively as a sequence of convex semidefinite programs.

Example 4 **Ring Oscillator Circuit Example**

Consider the n-stage ring oscillator whose dynamics are given by:

$$\begin{aligned}
\dot{x}_1^k &= -\eta_1 x_1^k - \alpha_1 \tanh(\beta_1 x_n^k) + w_1^k \\
\dot{x}_2^k &= -\eta_2 x_2^k + \alpha_2 \tanh(\beta_2 x_1^k) + w_2^k \\
&\vdots \\
\dot{x}_n^k &= -\eta_n x_n^k + \alpha_n \tanh(\beta_n x_{n-1}^k) + w_n^k,
\end{aligned} \tag{3.51}$$

with coupling between corresponding nodes of each circuit. Ring oscillators have found wide application in biological oscillators such as the repressilator in [6]. The parameters $\eta_k = \frac{1}{R_k C_k}$, α_k, and β_k correspond to the gain of each inverter. The input is given by:

$$w_i^k = d_i \sum_{j \in \mathcal{N}_{k,i}} (x_i^j - x_i^k), \tag{3.52}$$

where $d_i = \frac{1}{R^{(i)} C_i}$ and $\mathcal{N}_{k,i}$ denotes the nodes to which node i of circuit k is connected. We wish to determine if the solution trajectories of each set of like nodes of the coupled ring oscillator circuit given by (3.51)–(3.52) synchronize, that is:

$$x_i^j - x_i^k \to 0 \text{ exponentially as } t \to \infty \tag{3.53}$$

for any pair $(j, k) \in \{1, \ldots, N\} \times \{1, \ldots, N\}$ and any index $i \in \{1, \ldots, n\}$.

For clarity in our discussion, we take $n = 3$ as in Fig. 3.1. We first write the Jacobian of the system (3.51), where we have omitted the subscripts indicating circuit membership:

$$J(x)\big|_{x=\bar{x}} = \begin{bmatrix} -\eta_1 & 0 & \gamma_1(\bar{x}_1) \\ \gamma_2(\bar{x}_2) & -\eta_2 & 0 \\ 0 & \gamma_3(\bar{x}_3) & -\eta_3 \end{bmatrix}, \tag{3.54}$$

with $\gamma_1(\bar{x}_1) = -\alpha_1\beta_1 sech^2(\beta_1\bar{x}_3)$, $\gamma_2(\bar{x}_2) = \alpha_2\beta_2 sech^2(\beta_2\bar{x}_1)$, and $\gamma_3(\bar{x}_3) = \alpha_3\beta_3 sech^2(\beta_3\bar{x}_2)$. Define the matrices

$$A_0 = \begin{bmatrix} -\eta_1 & 0 & 0 \\ 0 & -\eta_2 & 0 \\ 0 & 0 & -\eta_3 \end{bmatrix} \quad A_1 = \begin{bmatrix} 0 & 0 & -\alpha_1\beta_1 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$
$$A_2 = \begin{bmatrix} 0 & 0 & 0 \\ \alpha_2\beta_2 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix} \quad A_3 = \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & \alpha_3\beta_3 & 0 \end{bmatrix}. \tag{3.55}$$

Then it follows that $J(x)$ is contained in a convex box:

$$J(x) \in \text{box}\{A_0, A_1, A_2, A_3\}. \tag{3.56}$$

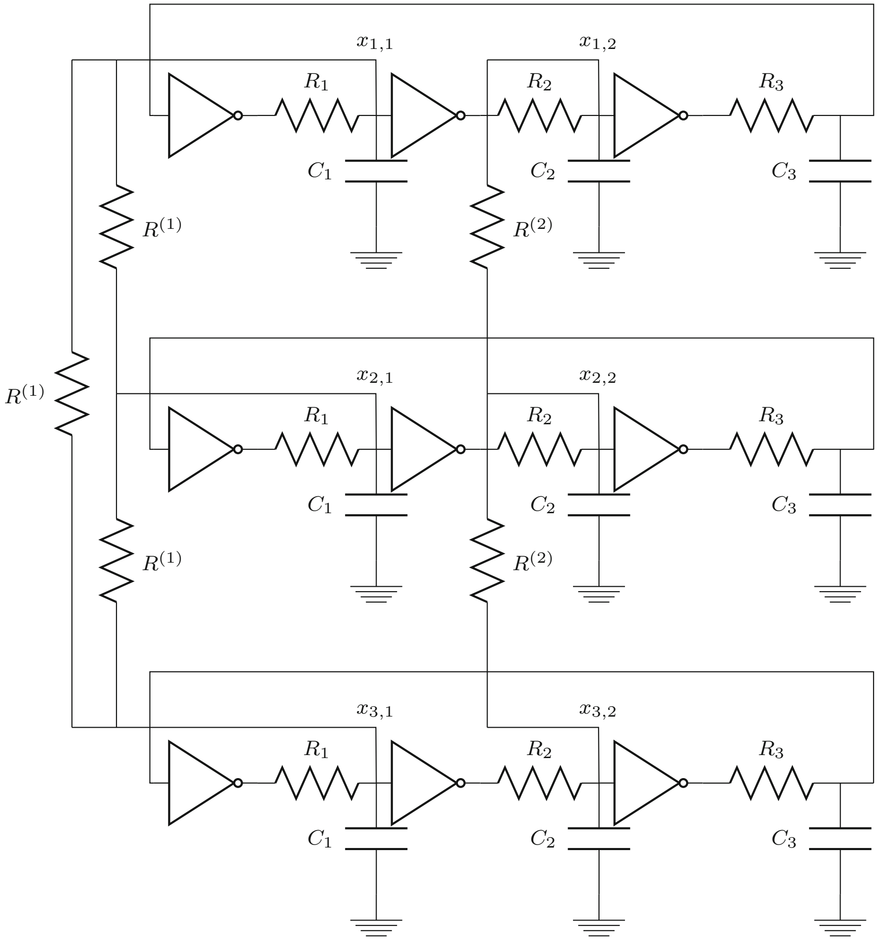

Fig. 3.1 An example of a network of interconnected three-stage ring oscillator circuits as in (3.51) coupled through nodes 1 and 2

While the method of Proposition 1 involves parametrizing a convex box as a convex hull with 2^p vertices, and potentially a prohibitively large linear matrix inequality computation, the problem structure can be exploited using Proposition 2 to obtain a simple analytical condition for synchronization of trajectories. In particular, the Jacobian of the ring oscillator exhibits a *cyclic* structure. The matrix M for which we seek a $\mathcal{Q}$ satisfying (3.49), or equivalently (3.46), is given by:

$$M = \begin{bmatrix} A_0 - \Lambda_2 - \frac{\mu}{2} I & B \\ C^T & -I \end{bmatrix}, \quad B = \begin{bmatrix} 0 & 0 & -\alpha_1\beta_1 \\ \alpha_2\beta_2 & 0 & 0 \\ 0 & \alpha_3\beta_3 & 0 \end{bmatrix}, \quad C = I_3. \quad (3.57)$$

Note that the matrix M exhibits a cyclic structure, and by a suitable permutation G of its rows and columns, it can be brought into a cyclic form $\tilde{M} = GMG^T$. Since $\tilde{M}$ is cyclic, it is amenable to an application of the *secant criterion* [2], which implies that the condition

$$\frac{\Pi_{i=1}^{3}\alpha_i\beta_i}{\Pi_{l=1}^{3}(\eta_l + \lambda_l + \frac{\mu}{2})} < \sec^3\left(\frac{\pi}{3}\right) \tag{3.58}$$

holds if and only if $\tilde{M}$ satisfies

$$\tilde{\mathcal{Q}}\tilde{M} + \tilde{M}^T\tilde{\mathcal{Q}} < 0 \tag{3.59}$$

with negative μ, for some diagonal $\tilde{\mathcal{Q}} > 0$. Pre- and post-multiplying (3.59) by G^T and G, respectively, (3.59) is equivalent to:

$$G^T\tilde{\mathcal{Q}}GM + M^TG^T\tilde{\mathcal{Q}}G < 0. \tag{3.60}$$

Thus, if $\tilde{\mathcal{Q}}$ is diagonal and satisfies (3.59), then $\mathcal{Q} = G^T\tilde{\mathcal{Q}}G$ is diagonal and satisfies (3.46). We conclude that if the secant criterion in (3.58) is satisfied, then by Proposition 2, we have:

$$\sup_{(x,t)\in V\times[0,\infty)} (J_F(x,t) - \Lambda_2) \; < \; \frac{\mu}{2}.$$

Because $\mathcal{Q}$ is diagonal and positive, Q is diagonal and positive. Therefore:

$$QD_i + D_iQ \; > \; 0 \quad \text{for each } i = 1, \ldots, r.$$

Therefore, since $\mu < 0$, by Corollary 4, we get:

$$x_i^j - x_i^k \to 0 \text{ exponentially as } t \to \infty \tag{3.61}$$

for any pair $(j,k) \in \{1,\ldots,N\} \times \{1,\ldots,N\}$ and any index $i \in \{1, 2, 3\}$.

We note that the condition for synchrony that we have found recovers Theorem 2 in [7], which makes use of an input-output approach to synchronization [20]. We have derived the condition using Lyapunov functions in an entirely different manner from the input-output approach.

3.5 Conclusions

We have derived Lyapunov inequality conditions that guarantee spatial uniformity in the solutions of compartmental ODEs and reaction-diffusion PDEs even when the diffusion terms vary between species. We have used convex optimization to develop tests using linear matrix inequalities that imply the inequality conditions, and have applied the tests to several examples of biological interest.

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