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A New Sufficient Condition for Additive D-Stability and Application to Cyclic Reaction-Diffusion Models

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***Abstract*— Matrix A is said to be additively D-stable if $A-D$ remains Hurwitz for all nonnegative diagonal matrices D. In reaction-diffusion models, additive D-stability of the matrix describing the reaction dynamics guarantees stability of the homogeneous steady-state, thus ruling out the possibility of diffusion-driven instabilities. We present a new criterion for additive D-stability using the concept of compound matrices. We first give conditions under which the second additive compound matrix has nonnegative off-diagonal entries. We then use this Metzler property of the compound matrix to prove additive D-stability with the help of an additional determinant condition. This result is then applied to investigate stability of cyclic reaction networks in the presence of diffusion.**

I. Introduction

The concept of *diagonal stability* and its variants are commonly used in the study of dynamic models in economics, ecology, and control theory, as surveyed by Kaszkurewicz and Bhaya [1]. A square matrix A is said to be *diagonally stable* if there exists a diagonal matrix $S>0$ such that $A^TS+SA<0$. Two related properties that are less restrictive than diagonal stability but possibly more restrictive than the Hurwitz property of A are *multiplicative D-stability*, which means that DA is Hurwitz for all diagonal matrices $D>0$, and *additive D-stability*, which means that $A-D$ is Hurwitz for all diagonal $D\geq 0$.

Additive D-stability is particularly useful for the study of reaction-diffusion systems where the matrix A represents the linearization of the reaction dynamics at a steady-state. Denoting by D the diagonal matrix of diffusion coefficients for each species, Casten and Holland [2] showed that the stability of the reaction-diffusion PDE is determined by the simultaneous stability of the family of matrices $A-\lambda_kD$, where $\lambda_k\geq 0$, $k=1,2,3,\cdots$ are the eigenvalues for Laplace's equation with Neumann boundary condition on the given spatial domain. Additive D-stability thus guarantees stability of the spatially homogeneous steady-state and rules out the possibility of diffusion-driven instabilities which constitute the basis of Turing's mechanism for pattern formation [3], [4]. Wang and Li [5] further studied the connection between additive D-stability and reaction-diffusion models, and gave several algebraic sufficient conditions that guarantee either stability or instability in the presence of diffusion.

In this paper, we present a new sufficient condition for additive D-stability using the concept of *additive compound matrices* [6]–[8] defined below. The key property employed in this condition is a special sign structure of matrix A which ensures that its second additive compound matrix $A^{[2]}$ is *Metzler*; that is, the off-diagonal entries of $A^{[2]}$ are nonnegative. Among the systems that exhibit this sign structure are *cyclic* reaction networks with negative feedback, where the end product of a sequence of reactions inhibits the first reaction upstream. For this class of networks, [9] established stability of the homogeneous steady-state in the presence of diffusion using a *secant criterion* which, as shown in [10], is necessary and sufficient for diagonal stability of A. In the present paper we prove that for cyclic systems, A is additively D-stable if and only if it is Hurwitz, thus relaxing the secant condition employed in [9].

In Section II we reveal the sign structure of A that is necessary and sufficient for its second additive compound matrix $A^{[2]}$ to be Metzler. This result is of independent interest because, as further explained in Section II, the Metzler property of $A^{[2]}$ is also useful for several nonlinear stability tests where A represents the Jacobian linearization. In Section III we employ the Metzler property of $A^{[2]}$ to prove additive D-stability of A with the additional condition that $(-1)^n\det(A-D)>0$ for every non-negative diagonal matrix D. We then proceed to derive a determinant test for the minors of A which is equivalent to $(-1)^n\det(A-D)>0$ and may be easier to verify in applications. In Section IV we first review the connection between additive D-stability and stability of reaction-diffusion PDEs and, next, present an ODE analog of this result using a compartmental model. In Section V we apply the results of the previous sections to cyclic reaction-diffusion models.

II. When is the Second Additive Compound Matrix Metzler?

Definition 1. *Let $A = (a_{i,j}) \in \mathbb{R}^{n\times n}$. The second additive compound of A is the matrix $A^{[2]} = (b_{i,j})$ of order $\binom{n}{2}$ defined as follows: For $i = 1, \cdots, \binom{n}{2}$, let $(i) = (i_1, i_2)$ be the ith number in the lexicographic ordering of integer pairs (i_1, i_2) such that $1 \leqslant i_1 \leqslant i_2 \leqslant n$. Then,*

$$b_{i,j} = \begin{cases} a_{i_1,i_1} + a_{i_2,i_2} & \text{if } (i) = (j); \\ (-1)^{r+s} a_{i_r,j_s} & \text{if exactly one entry } i_r \text{ of } (i) \\ & \text{doesn't occur in } (j) \\ & \text{and } j_s \text{ doesn't occur in } (i); \\ 0 & \text{if neither entry from (i)} \\ & \text{occurs in (j).} \end{cases}$$

As an illustration, for $n = 2$ and 3, the second additive compound matrix of $A = (a_{i,j})$ is:

$$n = 2: \quad A^{[2]} = a_{11} + a_{22} \tag{1}$$

$$n = 3: \quad A^{[2]} = \begin{bmatrix} a_{11} + a_{22} & a_{23} & -a_{13} \\ a_{32} & a_{11} + a_{33} & a_{12} \\ -a_{31} & a_{21} & a_{22} + a_{33} \end{bmatrix} \tag{2}$$

The term *additive* compound matrix is due to the property $(A + B)^{[2]} = A^{[2]} + B^{[2]}$. If $\lambda_1, \cdots, \lambda_n$ are the eigenvalues of A, then the eigenvalues of $A^{[2]}$ are all possible sums of the form $\lambda_i + \lambda_j$, $1 \leqslant i < j \leqslant n$.

Additive compound matrices have been used by several authors to analyze stability properties of nonlinear systems. Muldowney [7] showed that a sufficient condition for a closed orbit $\gamma = \{p(t) : 0 \leqslant t \leqslant T\}$ of the system $\dot{x} = G(x)$ to be orbitally asymptotically stable is that the origin be asymptotically stable for the linear system $\dot{y} = DG(p(t))^{[2]} y$ where $DG(x)$ denotes the Jacobian of $G(x)$. Using this orbital stability test, Li and Wang [11] proposed a technique to prove global asymptotic stability of the equilibrium for systems that possess a "Poincaré-Bendixson Property" whereby compact omega limit sets that contain no equilibria are closed orbits. This proof technique first uses Muldowney's test [7] to show that if periodic orbits exist then they are orbitally stable. It then makes use of the Poincaré-Bendixson Property to contradict the existence of periodic orbits when there is a unique asymptotically stable equilibrium. Sanchez [12] and Wang *et al.* [13] applied this technique to *cyclic* and *tridiagonal* feedback systems, respectively, which indeed possess the Poincaré-Bendixson Property as proven by Mallet-Paret and Smith [14] and Mallet-Paret and Sell [15].

An important step for proving orbital stability of periodic orbits in [12] and [13] is to show that the second additive compound matrix is Metzler for cyclic and tridiagonal matrices with negative feedback. In Theorem 1 below we give a full characterization of the class of matrices whose second additive compounds are Metzler, thus broadening the classes studied in [12] and [13]. This result is also instrumental for the additive D-stability criterion derived in the next section.

Theorem 1. *Let $A = (a_{i,j}) \in \mathbb{R}^{n\times n}$. Then $A^{[2]}$ is Metzler if and only if the off-diagonal elements of A satisfy:*

$$a_{i,j\ i\neq j} = \begin{cases} \leqslant 0 & \text{if } i = 1,\ j = n \quad \text{or} \quad i = n,\ j = 1; \\ \geqslant 0 & \text{if } i = k,\ j = k+1 \text{ or } i = k+1,\ j = k, \\ & k = 1, \cdots, n-1; \\ = 0 & \text{otherwise.} \end{cases} \tag{3}$$

that is, A has the following sign structure:

$$A = \begin{bmatrix} * & + & 0 & \cdots & 0 & - \\ + & * & + & \ddots & & 0 \\ 0 & + & * & \ddots & \ddots & \vdots \\ \vdots & \ddots & \ddots & \ddots & \ddots & \vdots \\ 0 & & \ddots & \ddots & \ddots & + \\ - & 0 & \cdots & 0 & + & * \end{bmatrix}, \tag{4}$$

where "+" denotes non-negative elements, "−" denotes non-positive elements, and "" represents an arbitrary sign.*

Proof. From the construction of $A^{[2]}$, the nonzero off-diagonal coefficients of $A^{[2]}$ come from the following entries of A:

(1) $a_{1,n}$ and $a_{n,1}$, which enter $A^{[2]}$ when $(i) = (1,k)$, $(j) = (k,n)$ or $(i) = (k,n)$, $(j) = (1,k)$, where $k = 2, \cdots, n-1$. Thus, $b_{i,j} = (-1)^{1+2} a_{1,n}$ or $(-1)^{2+1} a_{n,1}$, and $b_{i,j} \geqslant 0$ means $a_{1,n} \leqslant 0$, $a_{n,1} \leqslant 0$.

(2) $a_{k,k+1}$ and $a_{k+1,k}$, which enter $A^{[2]}$ when $(i) = (l,k)$, $(j) = (l,k+1)$ or $(i) = (l,k+1)$, $(j) = (l,k)$, or $(i) = (k,m)$, $(j) = (k+1,m)$ or $(i) = (k+1,m)$, $(j) = (k,m)$, where $l = 1, \cdots, n-2$, $m = 3, \cdots, n$. Thus, $b_{i,j} = (-1)^{1+1} a_{k,k+1}$ or $(-1)^{2+2} a_{k,k+1}$ or $(-1)^{1+1} a_{k+1,k}$ or $(-1)^{2+2} a_{k+1,k}$, and $b_{i,j} \geqslant 0$ means $a_{k+1,k} \geqslant 0$, $a_{k,k+1} \geqslant 0$.

(3) a_{i_r,j_s}, $i_r < j_s$, $(i_r, j_s) \neq (1,n)$, $(k,k+1)$, $k = 1, \cdots, n-1$. Because i_r and j_s cannot be consecutive integers, there exists at least one integer l such that $i_r < l < j_s$ and, thus, $(i) = (i_r, l)$ and $(j) = (l, j_s)$ yield $b_{i,j} = -a_{i_r,j_s}$. Because $(i_r, j_s) \neq (1,n)$, there exists an integer m such that either $m < i_r$ or $m > j_s$ holds. For $m < i_r$, $i = (m, i_r)$ and $j = (m, j_s)$ yield $b_{i,j} = a_{i_r,j_s}$. Likewise, for $m > j_s$, $i = (i_r, m)$ and $j = (j_s, m)$ give $b_{i,j} = a_{i_r,j_s}$. Thus, a_{i_r,j_s} appears in the off-diagonals of $A^{[2]}$ with both positive and negative signs, which means that $A^{[2]}$ can be Metzler only if $a_{i_r,j_s} = 0$.

(4) a_{i_r,j_s}, $i_r > j_s$, $(i_r, j_s) \neq (n,1)$, $(k+1,k)$, $k = 1, \cdots, n-1$. As discussed in part (3), there exists at least one integer l such that $i_r > l > j_s$ and, thus, $(i) = (l, i_r)$ and $(j) = (j_s, l)$ yield $b_{i,j} = -a_{i_r,j_s}$. Because $(i_r, j_s) \neq (n,1)$, there exists an integer m such that either $m > i_r$ or $m < j_s$ holds. For $m > i_r$, $i = (i_r, m)$ and $j = (j_s, m)$ yield $b_{i,j} = a_{i_r,j_s}$. Likewise, for $m < j_s$, $i = (m, i_r)$ and

$j = (m, j_s)$ give $b_{i,j} = a_{i_r,j_s}$. Thus, $A^{[2]}$ can be Metzler only if $a_{i_r,j_s} = 0$. □

III. A Sufficient Condition for Additive D-Stability

In Theorem 2 below, we present a sufficient condition for additive D-stability by using Theorem 1 from the previous section and the following lemmas:

Lemma 1. ([8]) *A matrix A of order n is Hurwitz if and only if $A^{[2]}$ is Hurwitz and $(-1)^n \det(A) > 0$.*

Lemma 2. ([16]) *The Metzler matrix A is Hurwitz if and only if it is diagonally stable; that is, there exists a diagonal matrix $S > 0$ such that $AS + SA^T < 0$.*

Lemma 3. ([1]) *If a matrix A is diagonally stable, then it is additively D-stable; that is, $A - D$ is Hurwitz for all diagonal matrices $D \geq 0$.*

Theorem 2. *Suppose a matrix A of order n is Hurwitz and satisfies the following conditions:*

1) *$(-1)^n \det(A - D) > 0$ for every non-negative diagonal matrix D;*
2) *$P^{-1}AP$ satisfies the sign structure (4) for some $n \times n$ invertible matrix P with the property that, for any non-negative diagonal matrix D, $P^{-1}DP$ is also a non-negative diagonal matrix.*

Then A is additively D-stable.

Proof. Let $\bar{A} := P^{-1}AP$, $\bar{D} := P^{-1}DP$ and $\Delta := \bar{A} - \bar{D}$. Because $\bar{A}$ is Hurwitz and satisfies the sign structure (4), it follows from Lemma 1 and Theorem 1 that $\bar{A}^{[2]}$ is Hurwitz and Metzler. From Lemmas 2 and 3, this means that $\bar{A}^{[2]}$ is additively D-stable from which we conclude that $\Delta^{[2]}$ is Hurwitz because $\Delta^{[2]} = \bar{A}^{[2]} - diag\{\tilde{d}_1, \cdots, \tilde{d}_n\}$, where $\tilde{d}_i = \bar{d}_{i_1} + \bar{d}_{i_2}$, $(i) = (i_1, i_2)$ is the ith number in the lexicographic ordering of integer pairs (i_1, i_2). Since $(-1)^n \det(\Delta) = (-1)^n \det(\bar{A} - \bar{D}) = (-1)^n \det(P^{-1}(A - D)P) = (-1)^n \det(A - D) > 0$, Lemma 1 implies that Δ and, thus, $A - D$ is Hurwitz. □

Examples of similarity transformations P satisfying condition 2 in Theorem 2 include diagonal matrices and permutation matrices. Note that condition 1 is necessary for $A - D$ to be Hurwitz and, thus, it cannot be relaxed. Because it may be difficult to verify condition 2 for all diagonal non-negative matrices D, in Lemma 4 below we present an equivalent condition that does not depend on the choice of D. Instead, it relies on the sign properties of the principal minors of A:

Definition 2. ([5]) *Let I_k denote the set $I_k = \{(i_1, i_2, \cdots, i_k) | 1 \leqslant i_1 < i_2 < \cdots < i_k \leqslant n\}$. For any $J = (i_1, i_2, \cdots, i_k) \in I_k$, let $P_J(A)$ denote the $k \times k$ principle submatrix of A, where $i_1, i_2, \cdots, i_k$ are the row and column indices of $P_J(A)$. A is said to satisfy the minors condition if $(-1)^k \det(P_J(A)) \geqslant 0$ for all $J \in I_k$ and $1 \leqslant k \leqslant n$.*

Lemma 4. *Given a Hurwitz matrix A, $(-1)^n \det(A - D) > 0$ holds for every non-negative diagonal matrix D if and only if the minors condition in Definition 2 holds.*

Proof. The proof follows from a combination of ideas from [5], which are repeated here because the exact statement of Lemma 4 is not given in [5]. To show that the minors condition implies $(-1)^n \det(A - D) > 0$, we rewrite $\det(A - D)$ as a polynomial of the diagonal entries d_j of D:

$$\begin{aligned} \det(A - D) = {} & \det(A) + \\ & \sum_{k=1}^{n-1} (-1)^k \sum_{J \in I_k} \det(P_{J'}(A)) d_J + (-1)^n \prod_{j=1}^{n} d_j, \end{aligned} \tag{5}$$

where $J' = \{1, 2, \cdots, n\} \backslash J$ for $J \in I_k$ and $d_J = \prod_{j \in J} d_j$. For the second term in (5), the minors condition gives

$$\begin{aligned} & (-1)^n \left((-1)^k \sum_{J \in I_k} \det(P_{J'}(A)) d_J \right) \\ & = (-1)^{2k} \left((-1)^{n-k} \sum_{J \in I_k} \det(P_{J'}(A)) d_J \right) \geq 0. \end{aligned} \tag{6}$$

Since A is Hurwitz, we note that $(-1)^n \det(A) > 0$ which, from (5), yields $(-1)^n \det(A - D) > 0$.

Next we prove that $(-1)^n \det(A - D) > 0$ implies the minors condition using a contradiction argument. Suppose $(-1)^n \det(A - D) > 0$ for every non-negative diagonal matrix D and that there exists $1 \leqslant k^* \leqslant n - 1$ such that $(-1)^{k^*} \det(P_J(A)) < 0$ for some $J \in I_{k^*}$. Choose $d_i = 0$ for $i \in J$ and $d_i = d > 0$ for $i \in J'$. Then, (5) becomes a polynomial in d, where the leading term is $(-1)^{n-k^*} \det(P_J(A)) d^{n-k^*}$. This means that, for sufficiently large d, the sign of $(-1)^n \det(A - D)$ is determined by

$$(-1)^n (-1)^{n-k^*} \det(P_J(A)) = (-1)^{k^*} \det(P_J(A)) < 0 \tag{7}$$

which contradicts the hypothesis that $(-1)^n \det(A - D) > 0$ for every non-negative diagonal matrix D. □

Wang and Li [5] proved that the minors condition, which we have shown in Lemma 4 to be equivalent to condition 1 of our Theorem 2, is sufficient for additive D-stability when the matrix order is $n \leq 3$. Thus, the complementary condition 2 in Theorem 2 is relevant only when $n > 3$.

IV. Additive D-Stability in Reaction-Diffusion Systems

Additive D-stability has been used to prove stability of reaction-diffusion PDEs with Neumann boundary conditions:

Lemma 5. ([2]) *Consider the reaction-diffusion model*

$$\frac{\partial x}{\partial t} = Ax + D\nabla^2 x \qquad \frac{\partial x}{\partial \nu} = 0 \tag{8}$$

where $x = x(t,\xi)$, the spatial variable ξ belongs to some bounded domain Ω with smooth boundary $\partial\Omega$, and $\frac{\partial x}{\partial \nu}$ denotes the directional derivative normal to $\partial\Omega$. Let $0 = \lambda_1 \leq \lambda_2 \leq \cdots \leq \lambda_k \leq \cdots$ and $\phi_k(\xi)$, $k = 1,2,3,\cdots$ denote the eigenvalues and eigenfunctions of Laplace's equation $\nabla^2\phi_k = -\lambda_k\phi_k$ in Ω with Neumann boundary condition $\frac{\partial \phi_k}{\partial \nu} = 0$. If, for each $k = 1,2,3,\cdots$, the eigenvalues of $A-\lambda_k D$ have negative real parts, then there exist positive constants K and ω such that, for all $t \geq 0$,

$$\|x(t,\xi)\| \leq Ke^{-\omega t}\|x(0,\xi)\| \tag{9}$$

where $\|x(t,\xi)\| := \sup_{\xi\in\Omega}|x(t,\xi)|$.

We now derive a complementary ODE result where we study n species evolving in N identical compartments. In the absence of coupling, the state vector $X_j \in \mathbb{R}^n$ for each compartment j is governed by:

$$\dot{X}_j = AX_j, \quad j = 1,\cdots,N. \tag{10}$$

Now let the compartments be interconnected according to a graph in which nodes represent compartments and edges represent the presence of diffusive coupling between them. Denoting by $L = (l_{i,j}) \in \mathbb{R}^{N\times N}$ the graph Laplacian matrix [17]:

$$l_{i,j} = \begin{cases} \text{number of nodes adjacent to node } i \text{ if } i = j \\ -1 \text{ if } i \neq j \text{ and node } j \text{ is adjacent to node } i \\ 0 \text{ otherwise,} \end{cases} \tag{11}$$

and by $D \in \mathbb{R}^{n\times n}$ the diagonal matrix of diffusion coefficients for each species, we obtain the coupled system:

$$\begin{bmatrix} \dot{X}_1 \\ \vdots \\ \dot{X}_N \end{bmatrix} = \begin{bmatrix} A & & \\ & \ddots & \\ & & A \end{bmatrix} \begin{bmatrix} X_1 \\ \vdots \\ X_N \end{bmatrix} - (L\otimes I_n) \begin{bmatrix} DX_1 \\ \vdots \\ DX_N \end{bmatrix}, \tag{12}$$

where $\otimes$ denotes the Kronecker product and I_n denotes the $n\times n$ identity matrix.

Theorem 3. *The eigenvalues of the system (12) are given by the eigenvalues of $A-\lambda_k D$, where $\lambda_k \geq 0$ is the k^{th} eigenvalue of the graph Laplacian L, $k = 1,\cdots,N$. In particular, if A is additively D-stable, then the coupled system (12) is Hurwitz.*

Proof. Two identities that will be used in the proof are:

1) $(A\otimes B)(C\otimes D) = (AC)\otimes(BD)$, when the sizes of A, C and B, D are compatible to form the products AC and BD;
2) $(I_p\otimes B)(C\otimes I_q) = C\otimes B$, where p is the number of rows of C and q is the number of columns of B.

From identity 1, system (12) can be reorganized as:

$$\dot{\mathbb{X}} = [I_N\otimes A - (L\otimes I_n)(I_N\otimes D)]\mathbb{X} = [I_N\otimes A - L\otimes D]\mathbb{X}, \tag{13}$$

where $\mathbb{X}$ denotes the concatenation of the vectors X_k. Let q_k, $k = 1,\cdots,N$ be the eigenvectors of L and λ_k be the corresponding eigenvalues: $q_k^T L = \lambda_k q_k^T$. Denoting

$$Z_k = (q_k^T\otimes I_n)\mathbb{X}, \tag{14}$$

we obtain from identity 1:

$$\begin{aligned} \dot{Z}_k &= (q_k^T\otimes I_n)[I_N\otimes A - L\otimes D]\mathbb{X} \\ &= [q_k^T\otimes A - (q_k^T L)\otimes D]\mathbb{X} \\ &= [q_k^T\otimes A - \lambda_k(q_k^T\otimes D)]\mathbb{X}. \end{aligned} \tag{15}$$

From identity 2,

$$\begin{aligned} q_k^T\otimes A &= A\cdot(q_k^T\otimes I_n), \\ q_k^T\otimes D &= D\cdot(q_k^T\otimes I_n), \end{aligned} \tag{16}$$

and, thus,

$$\dot{Z}_k = (A-\lambda_k D)Z_k, \quad k = 1,\cdots,N. \tag{17}$$

A general property of the graph Laplacian L is that $\lambda_1 = 0$, $q_1 = [1\cdots 1]^T$, $\lambda_k \geqslant 0$ for $k = 2,\cdots,N$. Thus, additive D-stability of A implies that the decoupled subsystems in (17) are each Hurwitz and, hence, (12) is also Hurwitz. □

As a special case of Theorem 3, consider two compartments connected by diffusion. The eigenvalues of the graph Laplacian

$$L = \begin{bmatrix} 1 & -1 \\ -1 & 1 \end{bmatrix} \tag{18}$$

are $\lambda_1 = 0$ and $\lambda_2 = 2$ and, thus, the eigenvalues of system matrix (12), rewritten here as

$$\begin{bmatrix} A-D & D \\ D & A-D \end{bmatrix}, \tag{19}$$

are given by the eigenvalues of A and A-2D. This example recovers Lemma 1 in [18], where a two-compartment model is transformed into

$$\begin{aligned} \dot{Z}_1 &= AZ_1 \\ \dot{Z}_2 &= (A-2D)Z_2 \end{aligned} \tag{20}$$

by choosing $Z_1 = X_1 + X_2$, $Z_2 = X_1 - X_2$. Equation (14) extends this decoupling change of coordinates to a general graph representing an arbitrary number of compartments.

V. Application to Cyclic Reaction Networks

We now apply the results of the previous sections to cyclic reaction networks, where the end product of a sequence of reactions activates or inhibits the first reaction upstream. To evaluate the local stability properties of cyclic reaction networks with inhibitory feedback, Tyson and Othmer [19] and Thron [20] studied the system matrix:

$$A = \begin{bmatrix} -a_1 & 0 & \cdots & 0 & b_n \\ b_1 & -a_2 & \ddots & & 0 \\ 0 & b_2 & -a_3 & \ddots & \vdots \\ \vdots & \ddots & \ddots & \ddots & 0 \\ 0 & \cdots & 0 & b_{n-1} & -a_n \end{bmatrix}, \tag{21}$$

where

$$a_i > 0, \quad i = 1, \cdots, n, \quad b_i > 0, \ i = 1, \cdots, n-1, \quad b_n < 0, \tag{22}$$

and showed that a sufficient condition for A to be Hurwitz is

$$\frac{-b_1 \cdots b_n}{a_1 \cdots a_n} < \sec(\pi/n)^n. \tag{23}$$

The "secant condition" (23) is also necessary for A to be Hurwitz when a_i's are identical; otherwise, it is more restrictive than the Hurwitz property.

In [10], the authors showed that (23) is a necessary and sufficient condition for A in (21)-(22) to be *diagonally stable* and exploited this property for a global stability analysis of the nonlinear reaction model. In [9], the diagonal stability property shown in [10] is employed to prove stability of the homogeneous steady-state $x(t,\xi) \equiv 0$ for the reaction-diffusion system (8) when A if of the cyclic form (21)-(22). In Theorem 4 below, we relax the secant condition (23) used in [9] by showing that the Hurwitz property of A is equivalent to additive D-stability for matrices in cyclic form. We prove this result for an arbitrary sign structure of the b_i parameters in (21):

Theorem 4. *A cyclic matrix of the form (21) with $a_i > 0$, $i = 1, \cdots, n$, is additively D-stable if and only if it is Hurwitz. Thus, if A is Hurwitz, the solutions of the reaction-diffusion equation (8) satisfy the stability estimate (9) for some positive constants K and ω.*

Proof. If $b_i = 0$ for some $i \in \{1, \cdots, n\}$, then the eigenvalues of A are its diagonal elements and, thus, A is additively D-stable whenever it is Hurwitz. If $b_i \neq 0$, $i = 1, \cdots, n$, then the diagonal similarity transformation $P = diag\{p_1, \cdots, p_n\}$ with $p_1 = 1$, $p_k = \prod_{i=1}^{k-1} \mathrm{sgn}(b_i)$, $k = 2, \cdots, n$, brings A to the form

$$\bar{A} = P^{-1}AP = \begin{bmatrix} -a_1 & 0 & \cdots & 0 & \delta|b_n| \\ |b_1| & -a_2 & \ddots & & 0 \\ 0 & |b_2| & -a_3 & \ddots & \vdots \\ \vdots & \ddots & \ddots & \ddots & 0 \\ 0 & \cdots & 0 & |b_{n-1}| & -a_n \end{bmatrix} \tag{24}$$

where $\delta = \mathrm{sgn}(b_1 \cdots b_n)$. If $\delta > 0$, then $\bar{A}$ is Metzler and, thus, additive D-stability follows from the Hurwitz property of A by Lemma 2. If $\delta < 0$, then $\bar{A}$ obeys the sign structure (4), and

$$(-1)^n \det(A - D) = (a_1 + d_1) \cdots (a_n + d_n) - b_1 \cdots b_n > 0 \tag{25}$$

for every non-negative diagonal matrix D because $b_1 \cdots b_n < 0$. Additive D-stability thus follows from the Hurwitz property of A by Theorem 2, and stability of the reaction-diffusion system (8) follows from Lemma 5. $\square$

A significant example that exhibits the cyclic form (21) is the "repressilator" design of Elowitz and Leibler [21], which is a synthetic genetic regulatory network consisting of three genes, where each gene inhibits the transcription of the next gene in the cycle by expressing a repressor protein. Denoting by x_{2i-1} the messenger RNA concentration for the i^{th} gene $i = 1,2,3$, and by x_{2i} the concentration of repressor protein expressed by this gene, we obtain a system matrix of the form (21) with $n = 6$ where $b_{2i-1} > 0$ and $b_{2i} < 0$, $i = 1,2,3$. It thus follows from Theorem 4 that, if this matrix is Hurwitz, then it is additively D-stable and thus stability of the homogeneous steady-state is guaranteed in the presence of diffusion. An interesting question is what happens in the situation where the linearization of this reaction network model is unstable and the trajectories converge to a limit cycle as suggested by the experimental results in [21]. We are currently investigating whether in this case diffusion would lead to spatially synchronized oscillations.

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