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Analysis and Design of Delayed Genetic Regulatory Networks

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To Chunyan and Ruitong

Xian Zhang

To My Family

Yantao Wang

To My Family

Ligang Wu

Preface

The research on genetic regulatory networks (GRNs) is multi-disciplinary, crossing biology, control science, computer science, electronic science mathematics, theoretical physics, etc. In the last two decades, mathematical models have become a powerful tool for studying of GRNs. In general, mathematical models of GRNs are divided into two classes: the discrete models and the continuous ones. In the continuous models, the variables describe the concentrations of mRNAs and proteins as continuous values, which can provide detailed understanding of the nonlinear dynamical behavior exhibited by GRNs. Recently, it has been shown that differential equation models including delayed states, named as delayed GRNs, can more accurately describe GRNs. As a result, much effort has been paid to the study of delayed GRNs, and many significant results have been reported in literature. From the point of control theory, the research on delayed GRNs includes mainly two aspects: analysis and design. In spite of the fact that there exist some Ph.D. theses related to delayed GRNs, there is no comprehensive book on this topic.

The aim of this book is to provide an introduction for current advances of delayed GRNs and present the basic methods for analysis and design of delayed GRNs. The whole book is divided into 11 chapters and focuses on the analysis and design problems on continuous-time delayed GRNs except the last chapter. All the contexts are taken from the authors' publications. This book is also intended to offer a collection of important references on analysis and design of delayed GRNs.

The book is addressed to graduate students and research-level mathematicians. It is hoped that the book will be suitable for postgraduate use or as a reference.

Many researchers in the world have made great contribution to analysis and design of delayed GRNs. Due to the length limitation and the structural arrangement, many of their published results are not included in the book. I would extend my apologies to these researchers.

I would appreciate any comments and corrections from the readers. Please feel free to contact me by the e-mail: xianzhang@hlju.edu.cn.

Harbin, China
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Xian Zhang

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Two co-authors of this book and I have cooperated to study delayed GRNs for 5 years at least. My colleagues, Dr. Xiangyu Gao, Dr. Yu Xue, Dr. Jing ma, Dr. Yanjiang Li, and Dr. Guodong Zhang, and previous graduate students, Ms. Ahui Yu, Ms. Ying Zhou, Mr. Shaochun Cui, Ms. Tingting Yu, Ms. Jing Wang, Mr. Xingming Zhou, Ms. Jiahua Zou, Ms. Yuanyuan Han, Ms. Tingting Liu, and Ms. Xiaofei Fan, have put great efforts on research of delayed GRNs. My present graduate students, Mr. Ning Zhao, Ms. Xin Li, Ms. Haifang Li, Ms. Shasha Xiao, Ms. Xinxiao Liu, Ms. Lulu Sun, and Ms. Xinyue Zhang, all helped me to find the errors and typos in the manuscripts. Besides all the above, Ms. Xiaofei Fan has helped me with conducting a reasonable review of references, and Mr. Ning Zhao has helped me with the revision of mathematical symbols. Their help has greatly improved the quality of the manuscripts. Here, I would like to express my heartfelt appreciation of their contribution. My special thanks go to my wife Chunyan for her support during writing the book.

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Contents

Notations and Acronyms

$\mathbf{R}$	Field of real numbers
$\mathbf{R}^{n\times m}$	Set of all $n \times m$ matrices over $\mathbf{R}$
$\mathbf{R}^n$	Set $\mathbf{R}^{n\times 1}$
$\mathrm{diag}(x_1, \ldots, x_n)$ or D_x	Diagonal matrix
$\mathrm{col}(x_1, \ldots, x_n)$	Column vector
$\lambda_{\max}(A)$	Maximum eigenvalue of real symmetric matrix A
$\lambda_{\min}(A)$	Minimum eigenvalue of real symmetric matrix A
$\chi_j(A)$	Number of nonzero elements in the jth row of A
$\chi(A)$	diag $(\chi_1(A), \chi_2(A), \ldots, \chi_n(A))$
$\lvert A\rvert$	Matrix $\left[\lvert a_{ij}\rvert\right]$ with $A = \left[a_{ij}\right]$
$\prod$	Product sign
$\sum$	Sum sign
I_n or I	$n \times n$ identity matrix
$0_{m\times n}$ or 0	$m \times n$ zero matrix
A^{T}	Transpose of the matrix A
A^*	Conjugate transpose of the matrix A
$\det(A)$	Determinant of the square matrix A
$\mathrm{tr}(A)$	Trace of the square matrix A
$\rho(A)$	Spectral radius of the square matrix A
$\mathrm{sym}(A)$	Matrix $A + A^{\mathrm{T}}$
A^{-1}	Inverse of the nonsingular matrix A
$\langle m\rangle$	Set $\{1, 2, \ldots, m\}$
$\circ$	Hadamard produce
$X \geqslant Y$ or $Y \leqslant X$	$X - Y$ is real symmetric positive semi-definite
$X > Y$ or $Y < X$	$X - Y$ is real symmetric positive definite
$L_2[0, \infty)$	Set of square integrable functions over $[0, \infty)$
$\mathbf{J}$	Connected subset of $\mathbf{R}$
$C(\mathbf{J}, \mathbf{R}^n)$	Linear space of all continuous functions $h : \mathbf{J} \to \mathbf{R}^n$
$\lVert\cdot\rVert_2$	Euclidean norm on $\mathbf{R}^n$, or its induced norm

$\mathcal{C}((-\infty, 0], \mathbf{R}^n)$	Linear space of all bounded and uniformly continuous functions $\psi : (-\infty, 0] \to \mathbf{R}^n$
$\|\psi\|_{\mathcal{C}}$	Norm on $\mathcal{C}((-\infty, 0], \mathbf{R}^n)$ defined by $\|\psi\|_{\mathcal{C}} = \sup_{-\infty < s \leqslant 0} \|\psi(s)\|_2 + \int_{-\infty}^{0} \|\psi(s)\|_2 \mathrm{d}s$
$\mathcal{R}$	Compact set in $\mathbf{R}^l$
$\partial\mathcal{R}$	Boundary of $\mathcal{R}$
$C^1(\mathcal{R}, \mathbf{R}^n)$	Banach space of continuous differential functions mapping $\mathcal{R}$ into $\mathbf{R}^n$
$\|\cdot\|$	Norm on $C^1(\mathcal{R}, \mathbf{R}^n)$ defined by $\|y(x)\| = \left(\int_{\mathcal{R}} y^{\mathrm{T}}(x) y(x) \mathrm{d}x\right)^{1/2}$
$\|\cdot\|_d$	Norm on $C^1([-d, 0] \times \mathcal{R}, \mathbf{R}^n)$ defined by $\|\phi(t,x)\|_d = \max\left\{ \sup_{-d \leqslant t \leqslant 0} \|\phi(t,x)\|, \sup_{-d \leqslant t \leqslant 0} \left\|\frac{\partial \phi(t,x)}{\partial t}\right\|, \max_{1 \leq k \leq l} \sup_{-d \leqslant t \leqslant 0} \left\|\frac{\partial \phi(t,x)}{\partial x_k}\right\| \right\}$
$\mathbf{E}\{\cdot\}$	Mathematical expectation operator
$\mathcal{L}$	Weak infinitesimal operator
$A \preceq B$ or $B \succeq A$	Real matrices $A = [a_{ij}]$ and $B = [b_{ij}]$ satisfy $a_{ij} \leqslant b_{ij}$ for all i and j
$A \prec B$ or $B \succ A$	Real matrices $A = [a_{ij}]$ and $B = [b_{ij}]$ satisfy $a_{ij} < b_{ij}$ for all i and j

Next, we will briefly explain several phrases which are helpful to understand this book.

- The LKF is a class of nonnegative functionals acting on a space of functions.
- Jensen's inequality relaxes the integral term of quadratic quantities into the quadratic term of the integral quantities and results in a linear combination of positive functions weighted by the inverses of convex parameters.
- The free-weighting matrix approach introduces parameter matrices, indicating the relationship between the terms in the Leibniz–Newton formula, into LMIs to be solved.
- The convex technique simplifies LMIs, including a linear combination of finite items weighted by convex parameters, by using the property of convex functions.
- The reciprocally convex technique estimates the lower boundary of a combination of positive functions weighted by the inverses of convex parameters.
- The Wirtinger-type integral inequality is a class of inequalities that are a generalization of Jensen's inequalities and that are more accurate than Jensen's inequalities.
- A delay-dependent(-independent) result indicates solvable conditions to a problem on time-delay systems are (not) related to the information of delay.

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Chapter 1
Backgrounds

In this chapter we will briefly introduce some background knowledge related to Genetic Regulatory Networks (GRNs).

1.1 Introduction to GRNs

GRNs are collections of DNA segments in a cell which interact with each other indirectly through their mRNAs, protein expression products and other substances. The main processes of gene expression are gene transcription and translation of mRNAs. The research on GRNs is multi-disciplinary, crossing biology, control science, compute science, electronic science and theoretical physics, etc [30, 37, 42, 89, 91–93, 99]. Thus it is currently great interest to many students, scholars and experts (see [16, 17, 19, 20, 22, 82] and the references therein). With the appearance and development of DNA microarray technology [48], it has become possible to measure gene expression levels on a genomic scale, and further analyze GRNs. As a result, GRNs can help people understand the genome sequencing and the gene recognition.

Mathematical models have been used for the study of GRNs in the last two decades. As we know, weighting matrix model is the first model used in the research of GRNs. It represents the mutual regulation impact among genes, however, it leads to a great amount of computation because of the large number of genes and the weighting matrices [76]. In order to avoid it, Boolean algebraic model is established, based on this model, Boolean networks depending on Boolean functions provided a framework for describing the complex interactions among genes [2]. After that, correlation matrices are used to reconstruct GRNs from gene expression. In addition, correlation coefficient method had been successfully applied to selecting of Drug NC160 [21]. Based on it, Butte and Kohane established a network of relationships between genes and drugs [10]. Followed by it, linear combination model and

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functional differential equation model are used to simulate GRNs [15], which are more effective to describe the nonlinear dynamical behavior, however, it also leads to much more computation time than Boolean model.

The mathematical models of GRNs have become a powerful tool for studying genetic regulatory processes in living organisms, and they can be roughly divided into two types: the discrete models [2, 6, 11, 16, 22, 39, 54, 59, 75, 76] and the continuous models [12, 15, 17, 19, 28, 63, 74]. In the continuous models, the variables describe the concentrations of mRNAs and proteins as continuous values, which can provide detailed understanding of the nonlinear dynamical behavior exhibited by GRNs. Usually, a continuous model is described by a differential equation. However, in GRNs, mRNAs and proteins may be synthesized at different locations; thus, the transcription or the diffusion of mRNAs and proteins among these locations results in sizable delays [12]. Therefore, theoretical models without consideration of delay may even provide wrong predictions. So, differential equation models including delayed states, named as delayed GRNs, can more accurately describe GRNs, and hence it can better show the nature of life. As a result, much effort has been paid to the study of delayed GRNs, and many significant results have been reported in literature on the stability analysis [4, 39, 41, 53, 73, 90–92, 96], passivity analysis [42], Hopf bifurcation analysis [79, 85, 86], controller synthesis [14, 27, 30, 40], estimator design [44, 74, 89, 99], identifying unknown parameters [13, 62], design [33], and so on.

As we all known, stability is one of the most important properties for any dynamic system. So, it is important and necessary to analyze stability of delayed GRNs. There are mainly two methods to establish stability criteria for delayed GRNs: the linear matrix inequality (LMI) method [12, 36, 38, 52, 71, 73, 91] and the M-matrix method [64–66, 77, 78, 93]. The LMI method-based stability criteria are generally effective for reducing conservativeness, but they are computationally complex; while the M-matrix method-based stability criteria are more computationally simple, because they just need to verify whether a constant matrix is a nonsingular M-matrix.

Key points of the LMI method are the constructions of Lyapunov–Krasovskii functionals (LKFs) and the employments of analysis techniques, which determines the resultant stability criterion to be less or more conservative at a certain point. In order to reduce conservativeness of LMI method-based stability criteria, some useful approaches have been introduced, e.g., delay decomposition approach [87, 98], reciprocally convex combination approach [70], augmented LKF approach [69], free-weighting matrix approach [69, 80, 88, 97] and convex combination approach [88]. These approaches are generally available for reducing conservativeness, but they will also increase the number of LMIs or of variables in LMI(s), which results in the computational complexity. For this reason, a so-called M-matrix-based approach has been proposed in [66, 77, 78] to infer the stability for equilibrium points of delayed GRNs.

Since modeling GRNs is an approximate process, it is necessary to introduce uncertainties into GRN models. As a result, much effort has been paid to establish robust stability criteria of uncertain delayed GRNs, and many significant results have been reported in literature [34, 38, 52, 68, 73].

For individual molecules, since movement of mRNA from a transcription site to translation sites is an active process with a significant range of transport times, so it is significant and necessary to model GRNs by using functional differential equations with mixed (i.e., discrete and distributed) delays [26, 92]. In addition, it is too simple to express the movement of macromolecule in actual networks only with distributed delay [87]. And stability criteria for GRNs only with discrete (distributed) delays are generally unavailable for GRNs with mixed delays. For this reason, the stability analysis for equilibrium points of GRNs with mixed delays has received more and more attention of scholars (see [51, 55, 69, 70, 87, 88, 98] and the references therein). All of these stability criteria in these papers are established by using the LMI method.

It is worth noting that the Lyapunov asymptotic stability and finite-time stability are a pair of independent concepts: a finite-time stable system may not be Lyapunov asymptotically stable, and vice versa [29]. It is well known that Lyapunov asymptotic stability is concerned with the behavior of a system over an infinite interval of time, while finite-time stability is used to describe the behavior of a system over a fixed time interval [3]. Furthermore, a system which is Lyapunov asymptotically stable may have a bad transient performance [3], and an unpredictable transient nature can yield a bad effect in the engineering, and even cause a great loss. Therefore, it can be seen that finite-time stability plays an important role in the practical applications.

In some mathematical modeling, it is assumed that GRNs are spatially homogeneous, namely, the concentrations of mRNAs and proteins are homogenous in space at all times. However, in some cases, it is imperative to introduce reaction-diffusion terms into models of GRNs, because it is necessary to consider the diffusion of mRNAs and proteins [8, 9, 17, 24, 94]. To the best of authors' knowledge, the stability problem for delayed reaction-diffusion GRNs has been only studied in [24, 25, 43, 95]. Ma et al. [43] established delay-dependent asymptotic stability criteria. Ma et al.'s results have been gradually improved in [24, 25] by introducing novel LKF and utilizing Wirtinger-type integral inequality approach. The problem of finite-time robust stochastic stability analysis for uncertain stochastic delayed reaction-diffusion GRNs has been studied in [95].

With changes in environment, the feedback loops which can inherently regulate the concentrations of mRNAs and proteins of GRNs may be destroyed. This will make GRNs' performance worse, and eventually lead to some fatal disease like cancer [1, 31, 84]. Therefore, it is necessary to adjust the feedback loops by artificial input control. For this end, the concentrations of mRNAs and proteins are needed. However, due to the complexity of GRNs, it is almost impossible to measure the exact concentrations. Hence, the state estimation for GRNs has been one of available methods to investigate dynamical behaviors. To the best of authors' knowledge, the state estimation problem for delayed reaction-diffusion GRNs is only in [89], although the reaction-diffusion-free case has been researched (see [5, 67, 74, 75] and the references therein).

1.2 Functional Differential Equation Models of GRNs

The following functional differential equations have been used to model GRNs with time-varying feedback regulation delays and translational delays [12, 52]:

$$\dot{m}_i(t) = -a_i m_i(t) + \varrho_i(p(t-\sigma_i(t))),\ t \geqslant 0,\ i \in \langle n\rangle, \tag{1.1a}$$

$$\dot{p}_i(t) = -c_i p_i(t) + d_i m_i(t-\tau_i(t)),\ t \geqslant 0,\ i \in \langle n\rangle, \tag{1.1b}$$

$$m_i(t) = \phi_i(t),\ p_i(t) = \psi_i(t),\ t \in [-d, 0],\ i \in \langle n\rangle, \tag{1.1c}$$

where $m_i(t)$ and $p_i(t)$ denote the concentrations of mRNA i and protein i at time t, respectively; a_i and c_i are positive real numbers that represent the rates of degradation of mRNA i and protein i, respectively; d_i is a positive real number that represents the translating rate from mRNA i to protein i; ϱ_i is a nonlinear function of the variables $p_i(t-\sigma_i(t))$ ($i \in \langle n\rangle$) which denotes the regulation function of gene i, and is monotonic with each variable; $\phi_i, \psi_i \in C([-d, 0], \mathbf{R})$, $d = \max\{\bar{\tau}, \bar{\sigma}\}$ with $\bar{\tau} = \max_{i\in\langle n\rangle}\bar{\tau}_i$ and $\bar{\sigma} = \max_{i\in\langle n\rangle}\bar{\sigma}_i$; $0 \leqslant \tau_i(t) \leqslant \bar{\tau}_i$ and $0 \leqslant \sigma_i(t) \leqslant \bar{\sigma}_i$ are continuously differentiable functions which denote the time-varying translational delay for mRNA i and the time-varying feedback regulation delay for protein i, respectively.

Note that when $n = 1$, GRN (1.1) degenerates into a single-gene network model, which has been proposed and investigated in [45].

Equation (1.1a) describes the transcriptional process, where ϱ_i characterizes the relative promoter or repressor activity of all possible proteins to mRNA i as a function of the concentrations of all possible proteins. Usually, one mRNA molecule or gene is generally activated or repressed by multiple proteins in the transcriptional process. This can be indicated by defining $\varrho_i(x) = \sum_{j=1}^{n}\varrho_{ij}(x)$ for all $x \geqslant 0$, which is called "SUM" logic [32]. Here, the regulation function ϱ_{ij} is a function of the Hill form as follows:

$$\varrho_{ij}(x) = \begin{cases} \frac{a_{ij}}{1+(x/b_j)^{h_j}}, & \text{if the transcription factor } j \\ & \text{represses gene } i, \\ 0, & \text{if the transcription factor } j \\ & \text{does not regulate gene } i, \\ \frac{a_{ij}(x/b_j)^{h_j}}{1+(x/b_j)^{h_j}}, & \text{if the transcription factor } j \\ & \text{activates gene } i, \end{cases}$$

where a_{ij} is the dimensionless transcriptional rate of transcription factor j to gene i, which is a nonnegative and bounded constant, b_j is a positive scalar, and h_j is the Hill coefficient that represents the degree of cooperativity.

Under the SUM logic, the general form of $\varrho_i(p(t-\sigma_i(t)))$ in (1.1a) is $\varrho_i(p(t-\sigma_i(t))) = \sum_{j=1}^{n} w_{ij}\varrho_{ij}(p_j(t-\sigma_{ij}(t)))$. In this book, we consider only the special

case $\varrho_i(p(t-\sigma_i(t))) = \sum_{j=1}^{n} w_{ij} g_j(p_j(t-\sigma_j(t)))$. From which, GRN (1.1) can be rewritten as:

$$\dot{m}_i(t) = -a_i m_i(t) + \sum_{j=1}^{n} w_{ij} g_j(p_j(t-\sigma_j(t))) + J_i,\ t \geqslant 0, \tag{1.2a}$$

$$\dot{p}_i(t) = -c_i p_i(t) + d_i m_i(t-\tau_i(t)),\ t \geqslant 0, \tag{1.2b}$$

$$m_i(t) = \phi_i(t),\ p_i(t) = \psi_i(t),\ t \in [-d, 0], \tag{1.2c}$$

where $i \in \langle n \rangle$,

$$w_{ij} = \begin{cases} -a_{ij}, & \text{if transcription factor } j \text{ represses gene } i, \\ 0, & \text{if transcription factor } j \text{ does not regulate gene } i, \\ a_{ij}, & \text{if transcription factor } j \text{ activates gene } i, \end{cases}$$

$$J_i = \sum_{j \in \mathbf{S}_i} a_{ij},\ \mathbf{S}_i = \{j : j \in \langle n \rangle, w_{ij} < 0\},\ g_j(x) = \frac{(x/b_j)^{h_j}}{1 + (x/b_j)^{h_j}}.$$

Clearly, g_j is a monotonically increasing function with saturation, and satisfies that for all distinct $x, y \in \mathbf{R}$,

$$g_j(0) = 0,\ 0 \leqslant \frac{g_j(x) - g_j(y)}{x - y} \leqslant k_j,\ j \in \langle n \rangle, \tag{1.3}$$

where

$$\begin{aligned} k_j :&= \max_{u \geqslant 0} \dot{g}_j(u) \\ &= \frac{(h_j - 1)^{(h_j-1)/h_j} (h_j + 1)^{(h_j+1)/h_j}}{4 b_j h_j} > 0. \end{aligned} \tag{1.4}$$

When all proteins have the same feedback regulation delay (i.e., $\sigma_j(t) \equiv \sigma(t)$), and all mRNAs have the same translational delay (i.e., $\tau_i(t) \equiv \tau(t)$), the model (1.2) simplifies into:

$$\dot{m}_i(t) = -a_i m_i(t) + \sum_{j=1}^{n} w_{ij} g_j(p_j(t-\sigma(t))) + J_i,\ t \geqslant 0, i \in \langle n \rangle, \tag{1.5a}$$

$$\dot{p}_i(t) = -c_i p_i(t) + d_i m_i(t-\tau(t)),\ t \geqslant 0, i \in \langle n \rangle, \tag{1.5b}$$

$$m_i(t) = \phi_i(t),\ p_i(t) = \psi_i(t),\ t \in [-d, 0], i \in \langle n \rangle. \tag{1.5c}$$

Rewriting GRN (1.5) into compact matrix form, we obtain

$$\dot{m}(t) = -Am(t) + Wg(p(t-\sigma(t))) + J, \tag{1.6a}$$

$$\dot{p}(t) = -Cp(t) + Dm(t-\tau(t)), \tag{1.6b}$$

$$m(s) = \phi(s),\ p(s) = \psi(s),\ s \in [-d, 0], \tag{1.6c}$$

where

$$A = \mathrm{diag}(a_1, a_2, \ldots, a_n),\ W = [w_{ij}]_{n\times n},$$

$$C = \mathrm{diag}(c_1, c_2, \ldots, c_n),\ D = \mathrm{diag}(d_1, d_2, \ldots, d_n),$$

$$m(t) = \mathrm{col}(m_1(t), m_2(t), \ldots, m_n(t)),\ p(t) = \mathrm{col}(p_1(t), p_2(t), \ldots, p_n(t)),$$

$$\phi(t) = \mathrm{col}(\phi_1(t), \phi_2(t), \ldots, \phi_n(t)),\ \psi(t) = \mathrm{col}(\psi_1(t), \psi_2(t), \ldots, \psi_n(t)),$$

$$g(p(t)) = \mathrm{col}(g_1(p_1(t)), g_2(p_2(t)), \ldots, g_n(p_n(t))),$$

$$J = \mathrm{col}(J_1, J_2, \ldots, J_n).$$

In Corollary 2.7 below, it will be shown that GRN (1.6) has at least one nonnegative equilibrium point. Let (m^*, p^*) be an equilibrium point of (1.6), that is, it is a solution of the following equations:

$$-Am^* + Wg(p^*) + J = 0,\ -Cp^* + Dm^* = 0. \tag{1.7}$$

For convenience, we shift the equilibrium point (m^*, p^*) to the origin by using the transformation $\tilde{m}(t) = m(t) - m^*$ and $\tilde{p}(t) = p(t) - p^*$, then we have

$$\dot{\tilde{m}}(t) = -A\tilde{m}(t) + Wf(\tilde{p}(t-\sigma(t))),\ t \geqslant 0, \tag{1.8a}$$

$$\dot{\tilde{p}}(t) = -C\tilde{p}(t) + D\tilde{m}(t-\tau(t)),\ t \geqslant 0, \tag{1.8b}$$

$$\tilde{m}(s) = \phi(s) - m^*,\ \tilde{p}(s) = \psi(s) - p^*,\ s \in [-d, 0], \tag{1.8c}$$

where $f(\cdot) = g(\cdot + p^*) - g(p^*)$.

From the relationship between g and f, one can easily find that f satisfies the following sector conditions:

$$f_j(0) = 0,\ 0 \leqslant \frac{f_j(s)}{s} \leqslant k_j,\ \forall 0 \neq s \in \mathbf{R},\ j \in \langle n \rangle, \tag{1.9}$$

where k_j is defined as in (1.4), and $f_j(s)$ is the jth entry of $f(s)$. Set $K = \mathrm{diag}(k_1, k_2, \ldots, k_n)$.

1.3 Preliminaries

This section introduces some existing results which will be used to present the main results in the later chapters.

1.3.1 Nonsingular M-Matrix

In this subsection we will give the concept of nonsingular M-matrix and several related conclusions.

Definition 1.1 [49] A matrix is said to be a Z-matrix if it is a real square matrix with non-positive off-diagonal elements.

A matrix A is said to be nonnegative (positive), denoted by $A \succeq 0$ ($A \succ 0$), if all of its elements are nonnegative (positive).

Definition 1.2 [49] A Z-matrix A is said to be an M-matrix if $A = sI - B$ for some nonnegative matrix B and scalar $s \geqslant \rho(B)$.

Definition 1.3 [49] A Z-matrix A is said to be a nonsingular M-matrix if $A = sI - B$ for some nonnegative matrix B and scalar $s > \rho(B)$.

Lemma 1.4 *[49] Let A be an $n \times n$ Z-matrix. Then the following statements are equivalent:*

(i) *A is a nonsingular M-matrix.*
(ii) *All of its eigenvalues have positive real parts.*
(iii) *A is nonsingular, and all elements of A^{-1} are non-negative.*
(iv) *A^{T} is a nonsingular M-matrix.*
(v) *There exists an n-dimensional vector $\gamma \succ 0$ such that $A\gamma \succ 0$.*

For a real matrix $A = [a_{ij}]$ in $\mathbf{R}^{m\times n}$, let $|A|$ represent the matrix $[|a_{ij}|]$ in $\mathbf{R}^{m\times n}$.

Lemma 1.5 *[77] If A_1, A_3 and A_4 are $n \times n$ positive diagonal matrices, A_2 is an $n \times n$ real matrix, then the matrix $\begin{bmatrix} A_1 & -|A_2| \\ -A_3 & A_4 \end{bmatrix}$ is a nonsingular M-matrix if and only if $A_1A_4 - A_3|A_2|$ is a nonsingular M-matrix.*

Due to Lemmas 1.4 and 1.5, one can easily obtain the following result.

Proposition 1.6 *Let $E \in \mathbf{R}^{n\times n}$, and let A, C, D and K be $n \times n$ positive diagonal matrices. Then the following statements are equivalent:*

(i) *$AC - DK|E|^{\mathrm{T}}$ is a nonsingular M-matrix.*
(ii) *$AC - |E|KD$ is a nonsingular M-matrix.*
(iii) *$AC - D|E|K$ is a nonsingular M-matrix.*

(iv) $\begin{bmatrix} A & -|E|K \\ -D & C \end{bmatrix}$ *is a nonsingular M-matrix.*

(v) $\begin{bmatrix} A & -D \\ -K|E|^{\mathrm{T}} & C \end{bmatrix}$ *is a nonsingular M-matrix.*

1.3.2 Inequalities

First, we introduce the so-called Schur complementary Lemma as follows.

Lemma 1.7 (Schur Complementary Lemma) *[7] Let*

$$S := \begin{bmatrix} S_{11} & S_{12} \\ S_{12}^{\mathrm{T}} & S_{22} \end{bmatrix}$$

be a real matrix of appropriate sizes, where $S_{11}^{\mathrm{T}} = S_{11}$ *and* $S_{22}^{\mathrm{T}} = S_{22}$. *Then the following statements are equivalent:*

(i) $S < 0$.
(ii) $S_{11} < 0$ *and* $S_{22} - S_{12}^{\mathrm{T}} S_{11}^{-1} S_{12} < 0$.
(iii) $S_{22} < 0$ *and* $S_{11} - S_{12} S_{22}^{-1} S_{12}^{\mathrm{T}} < 0$.

Second, the following conclusion is important to design filters for systems with unknown states. Its proof is similar to one of [18, Theorem 1].

Lemma 1.8 *For given matrices* $P^{\mathrm{T}} = P > 0$ *and* $Q^{\mathrm{T}} = Q > 0$, *the matrix inequality*

$$\begin{bmatrix} -P^{-1} & A \\ A^{\mathrm{T}} & -Q \end{bmatrix} < 0$$

holds if and only if there is a matrix R such that

$$\begin{bmatrix} P - R - R^{\mathrm{T}} & R^{\mathrm{T}} A \\ A^{\mathrm{T}} R & -Q \end{bmatrix} < 0.$$

Third, the following three lemmas involve inequalities with uncertainty.

Lemma 1.9 (Reciprocally Convex Inequality) *[56] For given matrices* $M_1^{\mathrm{T}} = M_1 \in \mathbf{R}^{n \times n}$, $M_2^{\mathrm{T}} = M_2 \in \mathbf{R}^{m \times m}$ *and* $X \in \mathbf{R}^{n \times m}$, *if*

$$\Theta := \begin{bmatrix} M_1 & X \\ X^{\mathrm{T}} & M_2 \end{bmatrix} \geqslant 0,$$

then

$$\operatorname{diag}\left(\frac{1}{\alpha}M_1, \frac{1}{1-\alpha}M_2\right) \geqslant \Theta,\ \forall \alpha \in (0,1).$$

Lemma 1.10 *[72] Let A, D, E, F and P be real matrices of appropriate sizes. If $P^{\mathrm{T}} = P > 0$ and $F^{\mathrm{T}}F \leqslant I$, then*

$$(A + DFE)^{\mathrm{T}}P(A + DFE) \leqslant A^{\mathrm{T}}(P^{-1} - \varepsilon^{-1}DD^{\mathrm{T}})^{-1}A + \varepsilon E^{\mathrm{T}}E$$

for any scalar $\varepsilon > 0$ satisfying $P^{-1} - \varepsilon^{-1}DD^{\mathrm{T}} > 0$.

Lemma 1.11 *[7] For given $U \in \mathbf{R}^{m\times n}$, $W \in \mathbf{R}^{p\times q}$ and $X^{\mathrm{T}} = X \in \mathbf{R}^{m\times m}$, set $\mathcal{S} = \left\{V \in \mathbf{R}^{n\times p} : V^{\mathrm{T}}V \leqslant I_p\right\}$. Then*

$$X + UVW + W^{\mathrm{T}}V^{\mathrm{T}}U^{\mathrm{T}} < 0,\ \forall V \in \mathcal{S}$$

if and only if there exists a scalar $\varepsilon > 0$ such that

$$X + \varepsilon^{-1}UU^{\mathrm{T}} + \varepsilon W^{\mathrm{T}}W < 0.$$

Last, we introduce some integral inequalities as follows.

Lemma 1.12 (Gronwall's Inequality) *[46] For given a scalar $a \geqslant 0$, and two non-negative and integrable functions $u(t)$ and $b(\cdot, t)$ over $[0, T]$ such that $\frac{\partial}{\partial t}b(\cdot, t) \geqslant 0$ and $b(t, t)$ exist, if*

$$u(t) \leqslant a + \int_0^t b(\xi, t)u(\xi)\mathrm{d}\xi,\ t \in [0, T],$$

then

$$u(t) \leqslant a\mathrm{e}^{\int_0^t b(\xi,t)\mathrm{d}\xi},\ t \in [0, T].$$

Lemma 1.13 (Wirtinger's Inequality) *[57] If a function $f \in C^1([a, b], \mathbf{R})$ satisfies $f(a) = f(b) = 0$, then*

$$\int_a^b f^2(v)\mathrm{d}v \leqslant \frac{(b-a)^2}{\pi^2}\int_a^b \dot{f}^2(v)\mathrm{d}v.$$

Lemma 1.14 (Jensen's Inequality) *For given an $n \times n$ matrix $M^{\mathrm{T}} = M > 0$, a pair of scalars a and b satisfying $b \geqslant a$, and an integral vector function $w : [a, b] \to \mathbf{R}^n$, the following inequalities hold:*

(i) *[23]* $(b-a)\int_a^b w^{\mathrm{T}}(s)Mw(s)\mathrm{d}s \geqslant \Psi_1^{\mathrm{T}}M\Psi_1$;

(ii) [61] $\frac{b^2-a^2}{2}\int_a^b\int_\theta^0 w^{\mathrm{T}}(s)Mw(s)\mathrm{d}s\mathrm{d}\theta \geqslant \Psi_2^{\mathrm{T}}M\Psi_2$;
(iii) [50] $\frac{b^3-a^3}{6}\int_a^b\int_\theta^0\int_\lambda^0 w^{\mathrm{T}}(s)Mw(s)\mathrm{d}s\mathrm{d}\lambda\mathrm{d}\theta \geqslant \Psi_3^{\mathrm{T}}M\Psi_3$.

Here $\Psi_1=\int_a^b w(s)\mathrm{d}s$, $\Psi_2=\int_a^b\int_\theta^0 w(s)\mathrm{d}s\mathrm{d}\theta$ *and* $\Psi_3=\int_a^b\int_\theta^0\int_\lambda^0 w(s)\mathrm{d}s\mathrm{d}\lambda\mathrm{d}\theta$.

Lemma 1.15 *[47] For given a pair of scalars a and b with* $a<b$, *an integral function* $w:[a,b]\to\mathbf{R}^n$, *and an* $n\times n$ *matrix* $M^{\mathrm{T}}=M>0$, *the following inequalities hold:*

$$\int_a^b w^{\mathrm{T}}(s)Mw(s)\mathrm{d}s \geqslant (b-a)[\Gamma_0^{\mathrm{T}}\ \ \Gamma_1^{\mathrm{T}}\ \ \Gamma_2^{\mathrm{T}}]\hat{M}[\Gamma_0^{\mathrm{T}}\ \ \Gamma_1^{\mathrm{T}}\ \ \Gamma_2^{\mathrm{T}}]^{\mathrm{T}},$$

$$\int_a^b\int_\theta^b w^{\mathrm{T}}(s)Mw(s)\mathrm{d}s\mathrm{d}\theta \geqslant (b-a)^2[\Gamma_3^{\mathrm{T}}\ \ \Gamma_4^{\mathrm{T}}]\tilde{M}[\Gamma_3^{\mathrm{T}}\ \ \Gamma_4^{\mathrm{T}}]^{\mathrm{T}},$$

where

$$\hat{M}=\mathrm{diag}(M,3M,5M),\ \ \tilde{M}=\mathrm{diag}(2M,16M),$$

$$\Gamma_1=\Gamma_0-2\Gamma_3,\ \ \Gamma_2=\Gamma_0-6\Gamma_3+12\Gamma_5,\ \ \Gamma_4=\Gamma_3-3\Gamma_5,$$

$$\Gamma_0=\frac{1}{b-a}\int_a^b w(s)\mathrm{d}s,\ \ \Gamma_3=\frac{1}{(b-a)^2}\int_a^b\int_\theta^b w(s)\mathrm{d}s\mathrm{d}\theta,$$

$$\Gamma_5=\frac{1}{(b-a)^3}\int_a^b\int_\theta^b\int_\lambda^b w(s)\mathrm{d}s\mathrm{d}\lambda\mathrm{d}\theta.$$

Lemma 1.16 *[47] For given a pair of scalars a and b with* $a<b$, *a derivative function* $w:[a,b]\to\mathbf{R}^n$, *and an* $n\times n$ *matrix* $M^{\mathrm{T}}=M>0$, *the following inequalities hold:*

$$\int_a^b \dot{w}^{\mathrm{T}}(s)M\dot{w}(s)\mathrm{d}s \geqslant \frac{1}{b-a}[\Omega_0^{\mathrm{T}}\ \ \Omega_1^{\mathrm{T}}\ \ \Omega_2^{\mathrm{T}}]\hat{M}[\Omega_0^{\mathrm{T}}\ \ \Omega_1^{\mathrm{T}}\ \ \Omega_2^{\mathrm{T}}]^{\mathrm{T}},$$

$$\int_a^b\int_\theta^b \dot{w}^{\mathrm{T}}(s)M\dot{w}(s)\mathrm{d}s\mathrm{d}\theta \geqslant [\Omega_3^{\mathrm{T}}\ \ \Omega_4^{\mathrm{T}}]\bar{M}[\Omega_3^{\mathrm{T}}\ \ \Omega_4^{\mathrm{T}}]^{\mathrm{T}},$$

$$\int_a^b\int_\theta^b\int_\lambda^b \dot{w}^{\mathrm{T}}(s)M\dot{w}(s)\mathrm{d}s\mathrm{d}\lambda\mathrm{d}\theta \geqslant \frac{3(b-a)}{2}\Omega_5^{\mathrm{T}}M\Omega_5,$$

where

$$\bar{M}=\mathrm{diag}(2M,4M),\ \ \Omega_0=w(b)-w(a),\ \ \Omega_1=w(b)+w(a)-2\Gamma_0,$$

$$\Omega_2=\Omega_0+6\Gamma_0-12\Gamma_3,\ \ \Omega_3=w(b)-\Gamma_0,$$

$$\Omega_4=w(b)+2\Gamma_0-6\Gamma_3,\ \ \Omega_5=w(b)-2\Gamma_3,$$

and $\hat{M}$, Γ_0 *and* Γ_3 *are defined as in Lemma 1.15.*

These inequalities in Lemmas 1.15 and 1.16 will be unitedly named as *Wirtinger-type integral inequality*.

1.3.3 Miscellanea

Lemma 1.17 (Brouwer's Fixed Point Theorem) *[58] Every continuous function from a convex compact subset of a Euclidean space to itself has a fixed point.*

Let $\mathcal{R}$ be a compact set in the vector space $\mathbf{R}^l$ with smooth boundary $\partial\mathcal{R}$. Let $C^1(\mathcal{R}, \mathbf{R}^n)$ be the Banach space of functions which map $\mathcal{R}$ into $\mathbf{R}^n$ and have the continuous first derivatives. We define a pair of norms on $C^1(\mathcal{R}, \mathbf{R}^n)$ and $C^1([-d, 0] \times \mathcal{R}, \mathbf{R}^n)$ by $\|\cdot\|$ and $\|\cdot\|_d$ as follows:

$$\|y(x)\| = \left(\int_{\mathcal{R}} y^{\mathrm{T}}(x)y(x)\mathrm{d}x\right)^{1/2}$$

and

$$\|\phi(t,x)\|_d = \max\{\sup_{-d\leqslant t\leqslant 0}\|\phi(t,x)\|, \sup_{-d\leqslant t\leqslant 0}\left\|\frac{\partial\phi(t,x)}{\partial t}\right\|, \max_{1\leqslant k\leqslant l}\sup_{-d\leqslant t\leqslant 0}\left\|\frac{\partial\phi(t,x)}{\partial x_k}\right\|\},$$

respectively.

Lemma 1.18 (Green's Second Identity) *[60] If $\mathcal{R}$ is a bounded C^1–open set in $\mathbf{R}^n$ and $\mu, \upsilon \in C^2(\partial\mathcal{R}, \mathcal{R})$, then*

$$\int_{\mathcal{R}} \mu\Delta\upsilon\mathrm{d}x = \int_{\mathcal{R}} \upsilon\Delta\mu\mathrm{d}x + \int_{\partial\mathcal{R}}\left(\mu\frac{\partial\upsilon}{\partial\overline{n}} - \upsilon\frac{\partial\mu}{\partial\overline{n}}\right)\mathrm{d}S,$$

where $\frac{\partial\upsilon}{\partial\overline{n}}$ and $\frac{\partial\mu}{\partial\overline{n}}$ are the directional derivatives of υ and μ in the direction of the outward pointing normal $\overline{n}$ to the surface element $\mathrm{d}S$, respectively.

Lemma 1.19 *[35] For a function $\Phi : [0, \infty) \longrightarrow \mathbf{R}$, if $\dot{\Phi}$ is bounded over the interval $[0, \infty)$ (that is, there is a constant $\alpha > 0$ satisfying $|\dot{\Phi}(t)| \leqslant \alpha$ for all $t \in [0, \infty)$), then Φ is uniformly continuous over the interval $[0, \infty)$.*

Lemma 1.20 *[35] For a function $\Phi : [0, \infty) \to \mathbf{R}$, if Φ is uniformly continuous and $\int_0^\infty \Phi(s)\mathrm{d}s < \infty$, then $\lim_{t\to\infty}\Phi(t) = 0$.*