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Review

A review of the Lurie problem and its applications in the medical and biological fields

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Abstract: This paper provided a review of the Lurie problem and its applications to control as well as modeling problems in the medical and biological fields, highlighting its connection with robust control theory, more specifically the works of Doyle, Skogestad, and Zhou. The Lurie problem involved the study of control systems with nonlinearities incorporated into the feedback loop. Providing a simpler and broader approach, this review returned to the Lurie problem, covering basic stability concepts and Aizerman's conjecture, establishing it as a special instance of the Lurie problem. The paper also explained the connection between the Lurie problem and robust control theory, which resulted in the establishment of new conditions for the Lurie problem. The principal contribution of this paper was a comprehensive review, utilizing the preferred reporting items for systematic reviews and meta-analyses (PRISMA) methodology of the applications of the Lurie problem in the medical and biological fields, demonstrating its significance in various domains such as medical device controllers, mechanical ventilation systems, patient-robot-therapist collaboration, tele-surgery, fluid resuscitation control, nanobiomedicine actuators, anesthesia systems, cardiac mechanics models, oncology cell dynamics, epidemiological models, diabetes modeling, population dynamics and neuroscience, including artificial neural networks (ANN). This article seeked to present the latest advancements in the Lurie problem, offering an update for researchers in the area and a valuable starting point for new researchers with several suggestions for future work, showcasing the importance of Lurie-type systems theory in advancing medical research and applications.

Keywords: problem of Lur'e; absolute stability; disease modeling; Aizerman conjecture; nonlinear systems; robust control
Mathematics Subject Classification: 34D23, 68T07, 92-10, 93-10, 93B36, 93C10, 93C35, 93D09

1. Introduction

The Lurie problem, originating in the 1940s from aircraft control systems [1], has made significant contributions to fields like control theory and robust control, with applications extending to areas like brain studies [2, 3]. Despite its historical impact and thousands of related papers, it is still an open challenge to find the necessary and sufficient conditions for absolute stability in broader cases. Given the long history of the Lurie problem, writing a systematic review on the topic could be quite challenging due to the extensive volume of material involved. However, the monograph due to Liao [4] provides a comprehensive and elegant examination of the Lurie problem in nonmedical and non-biological fields, focusing this paper specifically on those areas. On page 37, Liao highlights how the Lurie problem laid the basis of robust control theory, but this perception is not quite evident in the literature.

To solve the Lurie problem, methods like the Lyapunov functions, Nyquist criterion, and linear matrix inequalities (LMI) are used. Sufficient stability conditions are typically provided by the circle criterion [5], Popov criterion [6], and contraction analysis [7]. Notably, Popov's criterion has occasionally provided necessary and sufficient conditions [8]. Beginning in the 1950s and 1960s, Aizerman [9], Krasovskii [10], Popov [6], and Kalman [11] laid the groundwork. Since the 1980s, research has linked the Lurie problem to chaos [4, 12, 13], L_2-stability [14–16], μ-analysis [17–19], linear fractional transformation (LFT) [20], uncertain systems [21], Zames–Falb multipliers [22], linear parameter varying (LPV) systems [23, 24], and switched systems [25]. Recent works apply Lyapunov functions and LMI [12, 24, 26–28], and revisit past issues to propose new stability conditions [29]. The problem remains important in the field of aeronautics [30].

1.1. Contributions

In parallel, showing that the Lurie problem and robust control theory are mutually related, this paper presents an unprecedented review of the Lurie problem (or absolute stability theory) applied to control and modeling problems in the medical and biological area. This review shows the state of the art in the Lurie problem, helping new researchers to understand the problem and have a starting point in their investigations. Therefore, in bullets, the main contributions of this paper are presented:

• In the review of the Lurie problem, this work represents the Lurie problem in a simpler and broader approach so that the reader can understand the essence of this problem. This review covers the basic stability concepts involved, Aizerman's conjecture, and some well-known results due to [5, 6, 31] (they are Theorems 1–3). Dealing in particular with Aizerman's conjecture, this work represents it in a simpler way in dimension 2 and shows its relationship with the Lurie problem. It is then established that Aizerman's conjecture is a particular case of the Lurie problem.

• Section 4 is dedicated to explaining the connection of the Lurie problem (i.e., the absolute stability problem) to the robust control theory. This approach, together with the μ-analysis and synthesis theories, developed by Doyle [32–34], Zhou [35], and Skogestad [36], has been the main basis for discoveries of new necessary and sufficient conditions for the Lurie problem (for example, [37–43]). In special, the Theorem 6 is presented by the first time in an international high-impact journal. This theorem with its proof was presented only in the first author's doctoral thesis [38].

• The principal contribution of this paper is to give a review of the applications of the Lurie problem (or absolute stability problem) in the medical and biological field presented in Section 5.

1.2. Organization

This paper is structured in two main parts: a conceptual review of the Lurie problem in Sections 3 and 4, and a review of applications in the medical and biological fields in Section 5. Before, in Section 2, the methods used for selecting the studies are presented. Section 3 presents a conceptual review of the Lurie problem with the main topics on stability, Aizerman's conjecture, and some well-known theorems. Section 4 reviews the connection between the Lurie problem and the concept of robust control, presenting some recent results. The second part is covered by Section 5, presenting an exploration of applications of the Lurie problem in the medical and biological fields, as well as some discussion and suggestions for future work. Finally, Section 6 contains the conclusion, with some final considerations of the review carried out and some proposals for future work.

2. Methodology

A total of 96 references was included in this review, with the methodology organized in two parts: (1) a revision of the Lurie problem concepts and (2) a review of its applications in the medical and biological fields. The search strategy involved the use of keywords across SCOPUS (a bibliographic database created by the academic and scientific publisher Elsevier), web of science (WoS), and Google Scholar, as outlined in Table 1. Google Scholar was primarily used to gain a general overview of the work on the Lurie problem, with few articles selected from this database. Due to its search engine limitations, STRING_3 was created as an alternative to STRING_1. Table 2 details the keywords, strings, search fields, document types, and the number of documents found. The search was conducted on May 24, 2024.

Table 1. Strings of keywords for search.

Set	Keywords
STRING_1	"Lurie problem" OR "Lurie's problem" OR "Lur'e problem" OR "absolute stability" OR "absolutely stable" OR "Lurie systems" OR "Lurie control" OR "Lurie-type" OR "Lurie type" OR "type Lurie" OR "Lur'e systems" OR "Lur'e control" OR "Lur'e-type" OR "Lur'e type" OR "type Lur'e"
STRING_2	"health" OR "healthy" OR "cardiac" OR "heart" OR "cancer" OR "diagnostics" OR "diagnosis" OR "illness" OR "disease" OR "sickness" OR "ailment" OR "treatment" OR "medical" OR "cure" OR "neuroscience" OR "brain" OR "biological" OR "cardiology" OR "dermatology" OR "endocrinology" OR "gastroenterology" OR "hematology" OR "nephrology" OR "neurology" OR "oncology" OR "ophthalmology" OR "orthopedics" OR "otolaryngology" OR "ediatrics" OR "psychiatry" OR "pulmonology" OR "radiology" OR "rheumatology" OR "surgery" OR "urology" OR "geriatrics" OR "gynecology" OR "obstetrics" OR "anesthesiology" OR "pathology"
STRING_3	"absolute stability" OR "Lurie problem" OR "Lur'e problem"

2.1. Rationale for the selection of keyword strings

The selection of keywords in Table 1 is designed to capture both the theoretical and applied aspects of the Lurie problem. STRING_1 focuses on core terminology, including variations like

"Lur'e problem" and "absolute stability," to ensure comprehensive coverage of the mathematical and control theory literature, while targeting specific topics such as control design and stability analysis. STRING_2 shifts the focus to applications in medical and biological sciences, using health-related terms and specific disciplines (e.g., "cardiac", "oncology", "neurology") to cover studies where the Lurie problem is applied to biological systems. The inclusion of general medical terms broadens the search to capture interdisciplinary research that links theoretical aspects of the Lurie problem with practical implementations in medicine. STRING_3 provides a simplified version for broader searches in Google Scholar. This approach ensures a balanced inclusion of both theoretical and applied studies, aligning with the review's aim to connect the Lurie problem with real-world biomedical systems.

Table 2. Table relating works on applications of the Lurie problem in the respective medical and biological areas.

Databases	Search method	Types of documents	Search fields	Quantity found
SCOPUS	STRING_1 AND STRING_2	Article; Conference paper; Review; Conference review; Book chapter; Book; Short survey	Title; abstract; keyword	320
SCOPUS	STRING_1	Same as above	Same as above	4832
Web of Science	STRING_1 AND STRING_2	Article; Review Article; Proceeding Paper; Book Review; Editorial Material; Meeting Abstract; Early Access; Record Review	Title; abstract; keyword plus; author keywords	169
Web of Science	STRING_1	Same as above	Same as above	3586
Google scholar	STRING_3	All	All	74800

2.2. Review of the concepts of the Lurie problem

The first part of the review, which includes articles inserted in the Sections 1, 3, and 4, deals only with the Lurie problem. According to Table 2, the main databases (SCOPUS and WoS) showed a total of 8418 studies in terms of STRING_1. For a gray database (Google Scholar), 74800 studies were found under the terms of STRING_3. Although no screening was carried out, the values show a higher range of studies with terms related to the Lurie problem. In fact, it is a widely studied subject in applied mathematics and electrical and mechanical engineering. The criteria used to select the papers in this part of the review were the relevance of the work and compliance with the narrative review presented by the authors. In this narrative review, an attempt was made to present a timeline of research into the Lurie problem, as well as some of the papers considered most relevant.

2.3. Review of applications of the Lurie problem in the medical and biological fields

The second part of the review, focused on applications of the Lurie problem in biology and medicine, follows the preferred reporting items for systematic reviews and meta-analyses

(PRISMA) [44] methodology, which provides recommendations for systematic reviews to guarantee clarity and precision. Figure 1 illustrates the PRISMA 2020 diagram for this review, showing the process of sorting and selecting studies from SCOPUS and WoS using the search method "STRING_1 AND STRING_2". Table 2 describes the included literature and research fields. The primary inclusion criterion was papers addressing the Lurie problem (STRING_1) with applications in medical or biological contexts (STRING_2). Specific reasons for excluding papers are shown on the right side of the PRISMA diagram. Of the 370 articles initially located on the SCOPUS and WoS databases (duplicates were excluded, see Figure 1), only 34 met the criteria and were included in the review. Additionally, based on the authors' judgment, works [2, 3, 38] were added, resulting in 37 studies included in this part of the review, discussed in Section 5.

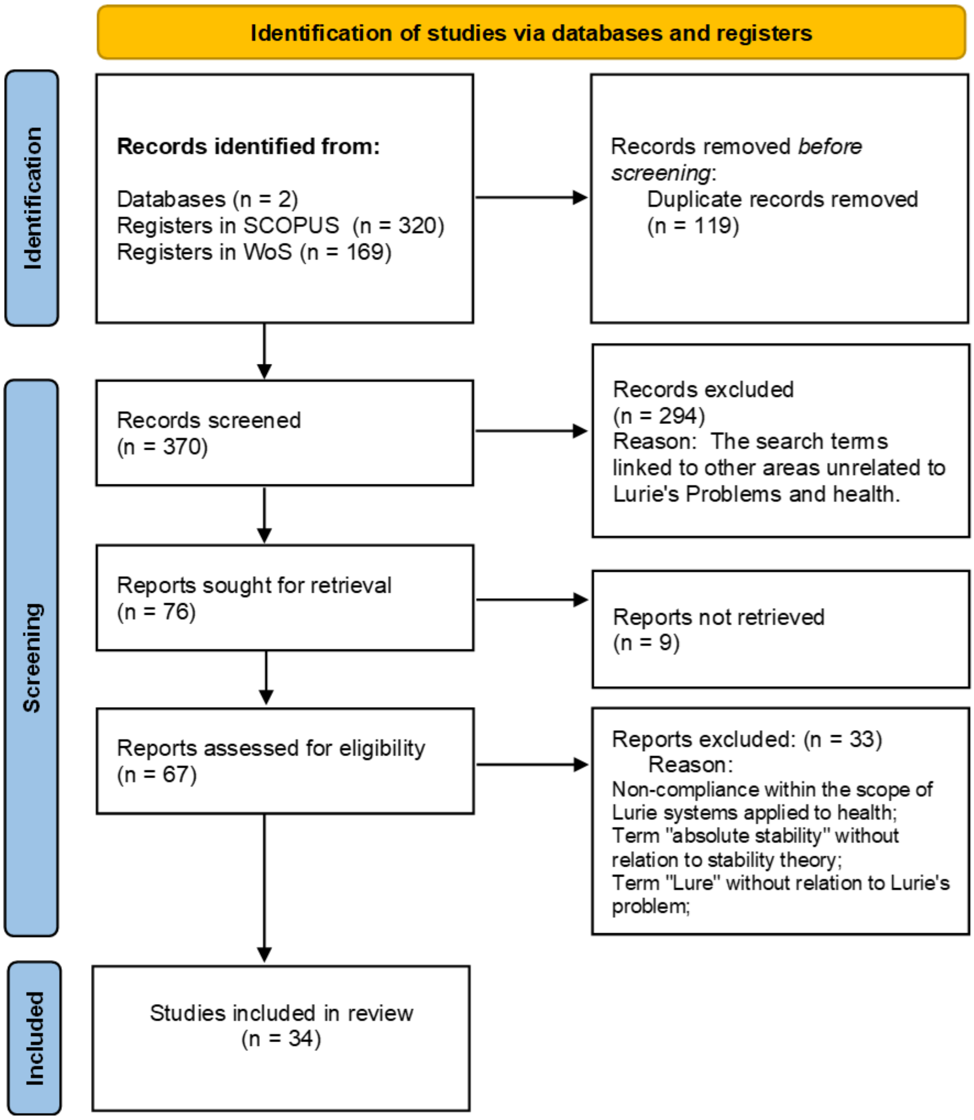


Figure 1. PRISMA flow diagram for review of applications of the Lurie problem in the medical and biological fields.

3. The Lurie problem

The origin of the Lurie problem is directly linked to an aircraft control problem, which also gave rise to the term absolute stability. Inherent to the Lurie problem, Lurie-type system arose, which in its simplest form has a linear part and a nonlinear part (see Figure 2a) in its feedback branch. The essence of the problem is to analyze the stability of the null solution (equilibrium point) of these systems, looking for necessary and sufficient conditions to guarantee global asymptotic stability (i.e., absolute stability).

Referring to the necessary and sufficient conditions for absolute stability means that without these conditions being met, achieving absolute stability is impossible. Necessary conditions must be present in any absolutely stable system, but they do not guarantee stability alone, whereas sufficient conditions ensure stability when satisfied, although they do not guarantee that they exist in all absolutely stable systems. In mathematical language, it is established as a necessary and sufficient condition by the "if, and only if," relation. Achieving conditions that are both necessary and sufficient, as done by Popov [6] and Zhang & Xian [8], is particularly difficult, requiring advanced mathematical tools like passivity, Lyapunov functions, LMI, contraction, Nyquist, and μ-analysis. While Lurie-type systems have evolved over time to encompass more complex forms, incorporating nonlinearities, delays, and uncertainties, the Lurie problem remains an active area of research due to its relevance across various fields like physics, mechanics, and biology and the new subproblems that continue to arise. This section provides a theoretical review of the Lurie problem, focusing on the original single-input-single-output (SISO) case and recent developments like the multiple-input-multiple-output (MIMO) case with delays. While not exhaustive or presenting the most general formulation, it aims to give a solid foundation for recognizing Lurie-type systems and applying existing techniques for the Lurie problem.

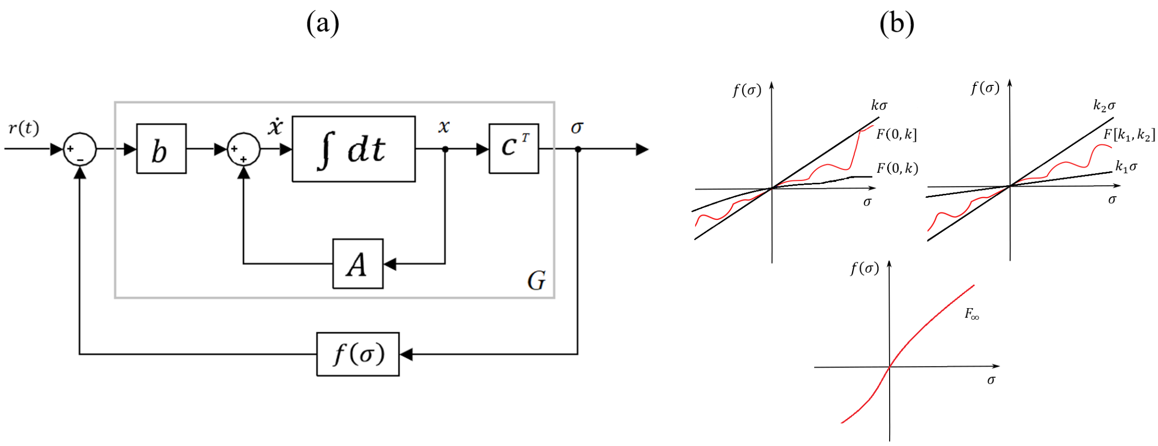


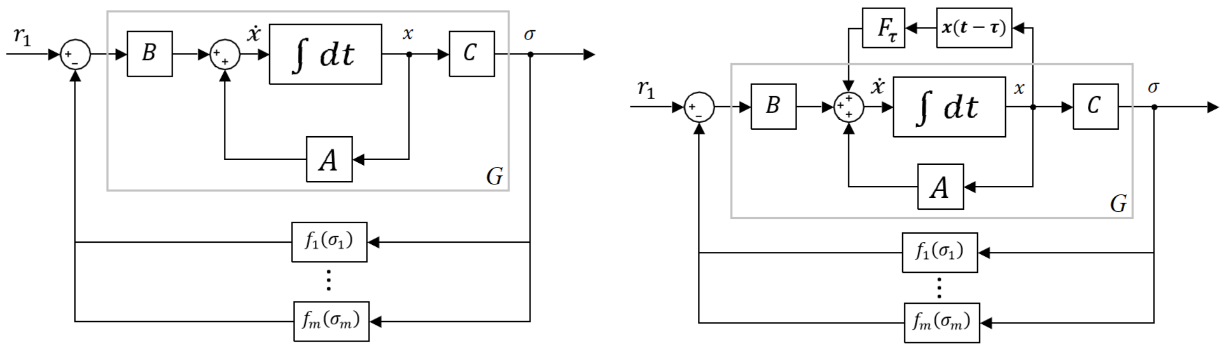
Figure 2. The problem Lurie in SISO case: (a) block diagram of the Lurie-type system in SISO case; (b) types of functions f.

3.1. Origin of the Lurie problem

Born in Mogilev, Belarus, Anatoly Isakovich Lurie (July 19, 1901–February 12, 1980) made significant contributions to the fields of mechanics and control theory, leaving a lasting legacy. The

Lurie problem, also known as the absolute stability problem, was introduced in the mid-1940s, prompted by challenges in aircraft automatic control [1]. The Lurie problem involves identifying necessary and sufficient conditions on the system parameters, for example, as depicted in Figure 2a, 3a or 3b, to ensure the stability of the global equilibrium point. Lurie explored a control problem related to aircraft during that era. The following is an idea of the aircraft control problem that Lurie studied in that period.

Fixed-wing aircraft utilize movable control surfaces to manage their flight, including ailerons, elevators, and rudders. Elevators are responsible for controlling the aircraft's upward or downward motion (pitch), ailerons manage the roll, and rudders handle directional changes (yaw), as illustrated in Figure 4.



(a) (b)

Figure 3. Block diagrams of the Lurie problem in MIMO case: (a) without delay; (b) with delay.

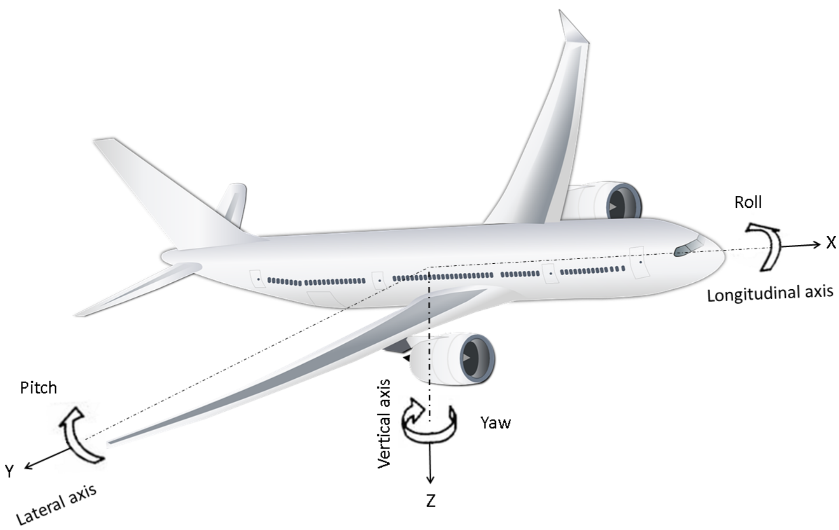


Figure 4. The three axes of rotation of an aircraft. Adapted from `https://stock.adobe.com/`.

In control, feedback is a core concept in the design of control systems. Figure 5a, presents this typical feedback structure, where $\bar{G}$ and K are linear systems represented by transfer functions. $\bar{G}$ represents the plant, which is the component to be controlled, and K denotes the controller in mathematical terms. According to [45], a transfer function serves as a mathematical model, offering an operational technique to describe the ordinary differential equations (ODE) that connects the input variable with the output variable.

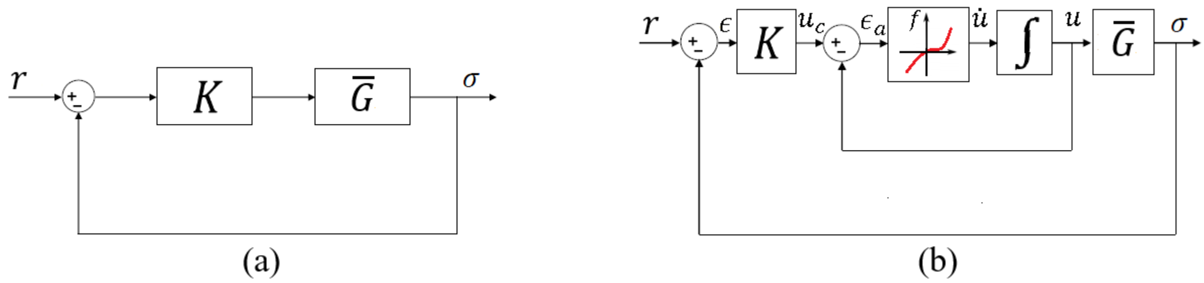


Figure 5. Control systems: (a) typical control system block diagram; (b) aircraft control system with rudder control.

An aircraft contains numerous feedback loops, as illustrated in Figure 5a. Some of these loops can be managed by the pilot, such as checking whether the actual route of the aircraft, σ, aligns with the desired route, r. Alternatively, this task can be handled by the autopilot system, which receives the input signal r, the direction set by the pilot. This signal often corresponds to the frequency of a ground-based station, such as a nondirectional beacon (NDB) or a very high frequency omnidirectional range (VOR)*, or even a radio station. The system continuously compares this direction with the aircraft's actual route, σ, and if there is any deviation, the control system K adjusts the position by acting on the control surfaces. However, some control loops, like the one depicted in Figure 5b, exhibit significant deviations from linearity. Automatic control loops in aircraft, which use control surfaces, are known to have nonlinearities, such as saturation of actuator. In these circumstances, u corresponds to the rudder deflection, and the control of the rudder seeks to keep the deviation u_c, defined by the controller K, until the deviation in the direction of the aircraft ϵ is corrected. Lurie solved this by separating the linear and nonlinear components of the differential equations of the model (detailed information in [46]).

3.1.1. Lurie-type system in the SISO case

Figure 2a shows a more general representation of such separation, where the linear dynamics are expressed in the system G and the $f(\sigma)$ function on the feedback represents the nonlinearity.

The Lurie problem in the SISO case involves determining the necessary and sufficient conditions for the system shown in Figure 2a to be globally asymptotically stable. Let $r = 0$, then the diagram in Figure 2a is represented by the system of differential equations shown in (3.1), known in the literature as Lurie-type system:

$$\begin{cases} \dot{x} = Ax - bf(\sigma), \\ \sigma = c^T x, \end{cases} \tag{3.1}$$

where $x \in \mathbb{R}^n$ represents the state vector, while $b, c \in \mathbb{R}^n$, $A \in \mathbb{R}^{nxn}$ are constant matrices. Typically,

*NDB or VOR are ground stations that transmit reference radio frequencies for aircraft navigation.

the nonlinearity $f(\sigma)$ is a continuous function constrained to lie within the first and third quadrants of the plane (see Figure 2b and Definition 1).

3.1.2. Lurie-type system in the MIMO case

Figure 3a illustrates the Lurie-type system block diagram in the MIMO case. In such cases, the nonlinear functions $f_j(\sigma_j)$ are more than one, making it a multi-input problem.

The diagram in Figure 3a is represented by the ODE system in (3.2):

$$\begin{cases} \dot{x} = Ax - Bf(\sigma) + Br_1, \\ \sigma = Cx, \end{cases} \tag{3.2}$$

where $x \in \mathbb{R}^n$ is the state vector, $f = [f_1, f_2, \cdots, f_m] \in \mathbb{R}^m$ is a vector of unknown but fixed functions and $\sigma \in \mathbb{R}^m$. Also, the matrices $B \in \mathbb{R}^{n\times m}$, $C \in \mathbb{R}^{m\times n}$ are known constants and $A \in \mathbb{R}^{n\times n}$ is Hurwitz (all the eigenvalues of the matrix have negative real part), known and fixed. The following definition precisely defines the f functions of the Lurie problem.

Definition 1. *The functions of the Lurie problem in the MIMO case are defined as the following (for the SISO case, just remove the index "j"):*

$$\begin{aligned}
&F_{(0,k_j]} := \{f_j | f_j(0) = 0, 0 < \sigma_j f_j(\sigma_j) \leq k\sigma_j^2, \sigma_j \neq 0\},\\
&F_{(0,k_j)} := \{f_j | f_j(0) = 0, 0 < \sigma_j f_j(\sigma_j) < k\sigma_j^2, \sigma_j \neq 0\},\\
&F_{[\underline{k}_j,\bar{k}_j]} := \{f_j | f_j(0) = 0, \underline{k}_j\sigma_j^2 \leq \sigma_j f_j(\sigma_j) \leq \bar{k}_j\sigma_j^2, \sigma_j \neq 0\},\\
&F_{\infty} := \{f_j | f_j(0) = 0, \sigma_j f_j(\sigma_j) > 0, \sigma_j \neq 0\}.
\end{aligned}$$

3.1.3. MIMO Lurie-type system with delay

The Lurie-type system under discussion is depicted in (3.3):

$$\begin{cases} \dot{x} = Ax - Bf(\sigma) + F_\tau x(t-\tau) + Br_1, \\ \sigma = Cx, \end{cases} \tag{3.3}$$

where $x \in \mathbb{R}^n$ is the state vector, $\tau > 0$ is the delay, $f(\sigma)$, and $\sigma \in \mathbb{R}^m$. $F_\tau \in \mathbb{R}^{n\times n}$, $B \in \mathbb{R}^{n\times m}$, $C \in \mathbb{R}^{m\times n}$ are all fixed matrices, and $A \in \mathbb{R}^{n\times n}$ is Hurwitz and fixed. The vector $r_1 \in \mathbb{R}^m$ can be an input signal. A block diagram of the system in (3.3) is shown in Figure 3b. Differential equations with delays are theoretically functional differential equations, but the operational methods using Laplace transform can equally be applied; on the other hand, initial conditions are not real numbers, but functions. The initial condition is defined by:

$$x(\theta) = \phi(\theta), \quad \theta \in [-\tau, 0], \quad \phi \in C[-\tau, 0]. \tag{3.4}$$

In the literature, there are many similar presentations of the Lurie problem with delay, for example, those formulated in [47, 48], as well as more complex problems with variable delays [49, 50].

3.1.4. Main categories Lurie-type systems

Generally, as mentioned by [4], Lurie-type systems can be divided into three categories:

(1) Direct: If the matrices A of the Figure 2a, 3a, or 3b are Hurwitz.

(2) Indirect: When the matrix A of Figure 2a, 3a, or 3b has an eigenvalue with a real part equal to zero and the other eigenvalues are negative real parts.

(3) Critical: If there is more than one eigenvalue of A with real part equal to zero and no eigenvalue with positive real part.

Remark 1. *Lurie-type systems are not limited to those shown in Figure 2a, 3a, or 3b. These are just some of the didactic examples of particular cases covered in this review. There are even more general forms of Lurie-type systems, for example, those discussed by [12, 26, 51], which consider non-autonomous systems (matrix A varying in time), uncertain matrix parameters, and time-varying delays.*

Remark 2. *Lurie-type system analysis often relies on software like Matlab or free alternatives like Octave. Matlab packages such as Robust Control Toolbox, Control System Toolbox, and Nonlinear Control Design Toolbox offer functions for Lurie-type systems, enabling the implementation of LMIs and frequency domain conditions. The specific Matlab function* ***popov*** *supports the analysis of certain Lurie-type systems. Notably, some of the results of this review, such as the Theorems 4–7, are employed using computational support (Matlab).*

3.2. Basic concepts of stability

This section clarifies the type of stability addressed by the Lurie problem. It introduces stability in the sense of Lyapunov, global asymptotic stability, and defines absolute stability, with definitions adapted from [4,36,45,52].

3.2.1. Stability in the sense of Lyapunov

Lyapunov stability is a fundamental concept in dynamical systems and underpins the definition of absolute stability. It applies to general autonomous systems described by a set of time-independent ODEs:

$$\begin{cases} \dot{x}(t) &= f(x(t)), \\ x(t_0) &= x_0, \end{cases} \tag{3.5}$$

where $f : D \subset \mathbb{R}^n \to \mathbb{R}^n$, fulfills the criteria that ensures the existence and uniqueness of solutions. Assume a solution is denoted by $x(t; t_0, x_0)$ and can extend to $[t_0, +\infty)$. If there exists a point x^* such that $f(x^*) = 0$, then $x(t; t_0, x^*) \equiv 0$ is the null solution or equilibrium point.

Definition 2. *The equilibrium point x^* of (3.5) is considered stable in the sense of Lyapunov if for every $\epsilon > 0$ there is $\delta > 0$ (where δ depends on ϵ), such that for every $x_0 \in D$ with $\|x_0 - x^*\| < \delta$ the following holds:*

$$\|x(t; t_0, x_0) - x^*\| \leq \epsilon, \forall t \in [t_0, +\infty). \tag{3.6}$$

Here, $\| \cdot \|$ represents a norm in $\mathbb{R}^n$.

Definition 3. *The equilibrium point x^* of (3.5) is called locally asymptotically stable if it is stable in Lyapunov sense and there exists $\eta > 0$, such that if $\|x_0 - x^*\| \leq \eta$ for all $x_0 \in D$, then*

$$lim_{t\to+\infty}\|x(t; t_0, x_0)\| = x^*. \tag{3.7}$$

Definition 4. *The equilibrium point x^* of (3.5) is called globally asymptotically stable if it is stable in Lyapunov sense, and for all $x_0 \in \mathbb{R}^n$ one has:*

$$lim_{t\to+\infty}\|x(t;t_0,x_0)\| = x^*. \tag{3.8}$$

Definition 5. *An equilibrium point which is not stable is called unstable, that is, if there exists x_0 such that, independently of how close it is to x^*,the trajectory moves away from the neighborhood of the ray ϵ at a finite time t, the point is unstable.*

3.2.2. Absolute stability

The absolute stability term originally is related to the Lurie-type system as, for example, presented by Eq (3.1), (3.2), or (3.3), but not limited to these (see Remark 1). Although Lurie proposed the concept of absolute stability for systems that later became known as Lurie-type systems, some works in the literature sometimes use the term absolute stability in a generalized manner to refer to the concept of global asymptotic stability for any type of system (as an example, see [45, pp. 160]). Below it is presented the definition of absolute stability for the MIMO case. In the SISO case, just consider $j = 1$.

Definition 6. ***(Absolute stability)*** *Assuming null input ($r_1 = 0$), it is said that the system (3.2) is absolutely stable if the zero solution of (3.2) is globally asymptotically stable in Lyapunov sense for $f_j(\sigma_j) \in F_{(0,k_j]}$, that is, $\forall\epsilon > 0$, $\exists\ \delta(\epsilon) > 0$, such that the solution $x(t) := x(t, t_0, x_0)$ of the initial value problem associated to (3.2) is unique and satisfies:*

$$\|x(t)\| = \sum_{j=1}^{m} |x(t)| < \epsilon, \quad \forall t \geq t_0, \quad if \quad \|x_0\| < \delta(\epsilon), \tag{3.9}$$

and for any $x_0 \in \mathbb{R}^n$:

$$\lim_{t\to\infty} \|x(t)\| = 0. \tag{3.10}$$

Remark 3. *Note that the definition of absolute stability indicates a unique equilibrium point. In fact, having a unique equilibrium point is a necessary condition for a system to achieve global asymptotic stability.*

Remark 4. *Considering the system (3.2) and the Definition 6, the formulation of the Lurie problem in the MIMO case is presented for $f_j(\sigma_j) \in F_{(0,k_j]}$. Similar definitions can also be formulated for other functions of the Definition 1.*

3.2.3. A particular case: Aizerman's conjecture

Throughout the development of the Lurie problem, Aizerman's conjecture or problem [9] initially stood out. An Aizerman-type system is a specific instance of a Lurie-type system [53]. In his conjecture, Aizerman proposed that the Hurwitz stability region coincides with the absolute stability sector [54]. While it was demonstrated that this conjecture holds true in the two-dimensional case, it was later shown to fail in higher dimensions [55], necessitating extra conditions. In general, these "extra conditions" are derived through the analysis of the Lurie problem.

In dimension 2, the Aizerman's conjecture can be formulated more clearly. Consider the system of ODEs below with constant coefficients $a, b, c, d \in \mathbb{R}$:

$$\begin{cases} \dot{x}_1 = ax_1 + bx_2, \\ \dot{x}_2 = cx_1 + dx_2, \end{cases} \tag{3.11}$$

where the characteristic polynomial of A is $p(\lambda) = \lambda^2 - (a + d)\lambda + (ad - bc)$. By the Routh-Hurwitz criterion, for the system (3.11) to be globally asymptotically stable in the Lyapunov sense, it must have: $ad - bc > 0$ and $a + d < 0$, or assuming that b, c, d are fixed and $d \neq 0$, then $\frac{bc}{d} < a < -d$. In other words, the graph of the line $\eta = a\xi$ in the plane (ξ, η) is in the angular region between $\eta = \frac{bc}{d}\xi$ and $\eta = -d\xi$.

Now suppose the replacement of the linear term ax_1 of (3.11) by another nonlinear term $f(x_1)$, where $f : \mathbb{R} \to \mathbb{R}$ is a continuous function such that $f(0) = 0$, so that $\frac{bc}{d}\xi < f(\xi) < -d\xi$ for $\xi \neq 0$, that is, f is one of the functions in Figure 2b. So, replacing the term ax_1 with $f(x_1)$, the following question arises: Is the trivial solution of (3.12) the same type of stability as before, i.e., is it globally asymptotically stable in the Lyapunov sense?

$$\begin{cases} \dot{x}_1 = f(x_1) + bx_2, \\ \dot{x}_2 = cx_1 + dx_2. \end{cases} \tag{3.12}$$

Similar problems can be formulated with the other terms:

$$\begin{cases} \dot{x}_1 = ax_1 + bx_2, \\ \dot{x}_2 = g(x_1) + dx_2. \end{cases} \tag{3.13}$$

Therefore, it is important to emphasize the Aizerman's conjecture can be seen as a particular case of the Lurie problem, for example, in Eq (3.12), the matrices of the Lurie problem (3.1) are:

$$x = \begin{pmatrix} x_1 \\ x_2 \end{pmatrix}, \; A = \begin{pmatrix} 0 & b \\ c & d \end{pmatrix}, \; b = \begin{pmatrix} 1 \\ 0 \end{pmatrix}, \; c' = \begin{pmatrix} 1 & 0 \end{pmatrix}.$$

Remark 5. *It is well-known that Aizerman's conjecture fails for systems of orders greater than 2. However, the study of the Lurie problem makes it possible to find the additional conditions for systems of higher orders to be absolutely stable (i.e., globally asymptotically stable for a Lurie-type system).*

3.3. Conventional theorems for the Lurie problem

This section introduces three fundamental theorems that offer sufficient conditions for ensuring absolute stability. These theorems represent renowned results for addressing the Lurie problem and employ widely recognized techniques in the field, including Lyapunov functions, passivities, Nyquist analysis, and LMIs. The first is the circle criterion of [5]. The second is Popov's criterion [6] for the SISO system, which, for certain classes of systems, provides the necessary and sufficient conditions for absolute stability. The third is the generalized Popov's criterion, due to Haddad [31], which brings condition from the frequency response for the MIMO Lurie system.

3.3.1. Circle criterion

Theorem 1. *Consider a linear time-invariant system, characterized by the transfer function* $G(s) = c^T(sI - A)^{-1}b$ *and a negative feedback with a static nonlinearity as on (3.1). Assume that the nonlinearity* $f(x)$ *is bounded by two known limits* $[k_1, k_2]$*, where* $0 \leq k_1 < k_2$*, if:* $k_1 \leq \frac{f(x)}{x} \leq k_2$*, for all* $x \neq 0$*, and*

$$\left|\frac{1 + k_2 G(j\omega)}{1 + k_1 G(j\omega)}\right| < 1,$$

for all $\omega \in \mathbb{R}$*, then the system is absolutely stable.*

Proof. It can be found in [5,56]. □

3.3.2. Popov criterion

Theorem 2. *Let* G_1 *and* G_2 *be real transfer functions and let* P *be a complex function, such that,* $G(j\omega) = G_1(\omega) + jG_2(\omega)$ *and* $P(j\omega) = G_1(\omega) + j\omega G_2(\omega)$*. If the system (3.1) satisfies the conditions:*

i. A *is Hurwitz and the pair* (A, b) *is controllable;*

ii. The nonlinearity f *belongs to the sector* $(0, k]$*;*

iii. $\exists\, q > 0$*,* $q \in R$*, such that,* $x - qy + \frac{1}{k} > P(j\omega)$*,* $\forall \omega \geq 0$*, wherein the complex plane* $x \in R$ *and* $y \in R$ *represent the real and imaginary axis, respectively; then, the zero solution (equilibrium point) of the system (3.1) is absolutely stable.*

Proof. It can be found in [56]. Moreover, in [57] one has a graphical interpretation. □

A practical example of this theorem can be found in [40].

3.3.3. Generalized Popov criterion

Theorem 3. *Let* $[0, k_j]$ *be the sectors that limit* $\tilde{f}_j(\tilde{\sigma}_j)$ *such that* $\tilde{f}_j \in F_{(0,k_j]}$ *and* $K = diag[k_j]$ *for* $j = 1, ..., m$*. If* $(\tilde{A}, \tilde{B})$ *is controllable,* $(\tilde{A}, \tilde{C})$ *is observable and there exists* $N = diag[n_j]$*, where* n_j *are nonnegative constants such that:*

$$Q(s) = K^{-1} + (I + Ns)\tilde{G}(s) > 0, \tag{3.14}$$

(i.e., Q *is strongly positive real), where* $\tilde{G}(s) = \tilde{C}(sI - \tilde{A})^{-1}\tilde{B}$*, then the zero solution of (3.2) is absolutely stable.*

Proof. It can be found in [31]. □

Remark 6. *According to [31],* $Q(s)$ *is strongly positive real if:*

i) $Q(s)$ *is asymptotically stable;*

ii) $H(j\omega) = Q(j\omega) - Q'(j\omega) > 0$ *for all real* ω*;*

iii) $H(\infty) = Q(\infty) - Q^T(\infty) > 0$*.*

A practical example of this theorem can be found in [39].

4. The relationship of the Lurie problem with robust control

The Lurie problem assumes that the nonlinearity resides within a specific sector, transforming it into a robustness issue aimed at determining stability conditions for nonlinearities within that sector. This involves identifying global asymptotic stability by analyzing system parameters and sectors, resulting in sufficient but often conservative conditions. In the MIMO context, the nonlinearity is represented as shown in Figure 6 and formulated in Eq (4.1), while the SISO case is elaborated in [40]. This allows the problem of absolute stability to be analyzed as a robust stability problem. To apply this concept, the definition of robust stability for the MIMO case is established:

Definition 7. *Assuming a null input ($r_1 = 0$), the uncertain but fixed system (4.1) is considered robustly stable if it remains asymptotically stable for any value of α_j within a specified interval, where the parameters $\alpha_j = [\alpha_1, ..., \alpha_m]$ are fixed but unknown real constants.*

Above it is presented a methodology used by [40, 41] for the SISO case. Here it is shown its extension to the MIMO case, as done by [39]. The objective is to substitute the unknown but fixed static nonlinearity f of (3.2) with a set of uncertain yet fixed linear functions $\alpha\sigma(x(t))$, where $0 < \alpha_j \leq k_j$ (see Figure 6). There are some classes of functions in the sector such that this approach is valid, that is, robust stability implies absolute stability. This leads to the formation of a corresponding set of plant models, represented as $G_p(s)$, which follows a standard procedure in robust control. Any nonlinearity is constrained and expressed within the limits of the first and third quadrants [58]. Consequently, the closed-loop linearized model of system (3.2) becomes:

$$\dot{x} = Ax + B(r_1 - \alpha Cx) \quad \rightarrow \quad \dot{x} = Ax + Br_1 - B\alpha Cx \quad \rightarrow \quad \dot{x} = (A - B\alpha C)x + Br_1.$$

Making $A_\alpha = (A - B\alpha C)$, one has:

$$\begin{cases} \dot{x} = A_\alpha x + Br_1, \\ \sigma = Cx. \end{cases} \tag{4.1}$$

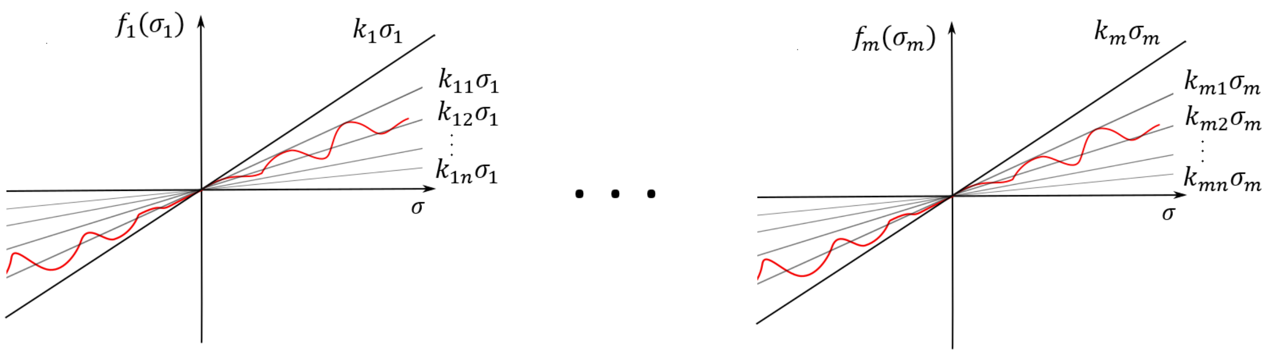


Figure 6. Mapping $0 < f_j(\sigma_j) \leq k_j\sigma_j$.

The following lemma is examined, an essential result adapted from [4, 52] and initially introduced in [39], which enables the analysis of absolute stability for the system (3.2) through the investigation of the robust stability of system (4.1). Here, a simple proof is presented, but the interested readers can find an in-depth content of the source of this theory in [52, pp. 190, Theorem 6.4.3] and [4, pp. 158, Theorem 7.4] from *sufficiency* onward. Therefore, the lemma below clarifies the connection between absolute stability and robust stability.

Lemma 1 ([39]). *For some class of functions in a sector, if the linear fixed and uncertain system (4.1) is robustly stable, then the system (3.2) is absolutely stable.*

Proof. Adding $(B\alpha\sigma - B\alpha\sigma)$ in (3.2), the equation can be rewritten as $\dot{x} = Ax + B\alpha\sigma - B\alpha\sigma - Bf(\sigma)$, and replacing σ by Cx, one has: $\dot{x} = (A - B\alpha C)x + B\alpha Cx - Bf(Cx)$. By applying Lagrange's formula, the solution $x(t, t_0, x_0)$ of (3.2) satisfies:

$$x(t) = e^{A_\alpha(t-t_0)}x_0 + \int_{t_0}^{t} e^{A_\alpha(t-\tau)} \underbrace{B[\alpha Cx(\tau) - f(Cx(\tau))]}_{F(\tau,x)} d\tau. \tag{4.2}$$

If the uncertain but fixed system (4.1) is robustly stable, then A_α is Hurwitz stable (with all eigenvalues having negative real parts) for all α within a certain interval. This implies the existence of constants $L \geq 1$ and $\beta > 0$ such that:

$$\|e^{A_\alpha(t-t_0)}\| \leq Le^{-\beta(t-t_0)}, \quad t \geq t_0. \tag{4.3}$$

This implies that the portion of the solution influenced by the initial condition asymptotically tends to zero. To guarantee that the integral term tends to zero, further conditions on $F(\tau, x)$ must be imposed. If the 2nd condition of Theorem 4.3 from [4] holds, then:

1) $\forall \epsilon > 0$, $\exists\, \delta(\epsilon) > 0$, and $t_1 \geq t_0$, such that $\|x_0\| < \delta(\epsilon)$ implies

$$\|x(t)\| = \|e^{A_\alpha(t-t_0)}x_0 + \int_{t_0}^{t} e^{A_\alpha(t-\tau)}B[\alpha Cx(\tau) - f(Cx(\tau))]d\tau\| < \epsilon;$$

and

2) for any $x_0 \in R$, one has

$$0 \leq \lim_{t\to\infty} \|x(t)\| \leq \lim_{t\to\infty} Le^{-\beta(t-t_0)} + \lim_{t\to\infty} \int_{t_0}^{t} Le^{-\beta(t-t_0)}B[\alpha Cx(\tau) - f(Cx(\tau))]d\tau = 0. \tag{4.4}$$

□

Thus, the results in this section are applicable to problems with the valid function classes, providing sufficient conditions for absolute stability. The following presents some recent results that provide absolute stability conditions for Lurie-type systems from robust control techniques that has its roots in the work developed by Doyle [32–34], Zhou [35] and Skogestad [36]. These results, taken from [39, 40], have a different approach from the traditional LMI and Lyapunov functions. Next, structured singular value (SSV) (or μ) is defined, which is a fundamental element for the next results. It is used to analyze the stability of a Lurie-type system in the form of LFT of Figure 7. LFT for application in the Lurie problem is presented in detail in [39].

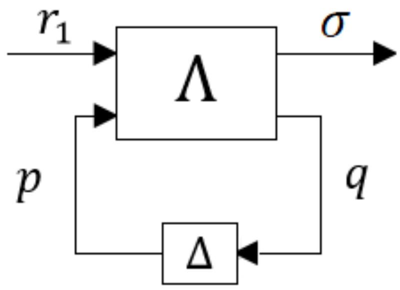


Figure 7. Λ-Δ-structure.

Definition 8 ([35]). *Consider a matrix M along with a structured set of matrices Δ satisfying the condition $\|\Delta\|_\infty \leq 1$. The SSV, commonly referred to as μ, is defined as a real nonnegative function given by:*

$$\mu_\Delta(M) \triangleq \frac{1}{min_\Delta\{\bar{\sigma}(\Delta)|det(I - M\Delta) = 0\}}. \tag{4.5}$$

Here, M represents a complex matrix (specifically, a matrix of transfer functions), and $\Delta = diag(\Delta_i)$ is a block diagonal matrix with the condition that $\bar{\sigma}(\Delta_i) \leq 1$. Some blocks may either be repeated or constrained to real values. If no such structured matrix Δ can be identified, then it follows that $\mu(M) = 0$.

The goal is to find Δ^* that minimizes $\bar{\sigma}(\Delta^*)$ subject to the constraint $det(I - M\Delta) = 0$. This is an optimization problem with constraints. The next lemma puts the system (4.1) according to Figure 7.

Lemma 2 ([39]). *The system (4.1) with $f_j \in F_{(0,k_j]}$ has a Δ-Structure given by $\Delta = \{diag[\delta_1, . . . , \delta_m] : |\delta_j| \leq 1\}$, with:*

$$\Lambda = \begin{bmatrix} A_0 & B_0 & E_1 & ... & E_m \\ C_0 & D_0 & F_1 & ... & F_m \\ G_1 & H_1 & 0 & ... & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ G_m & H_m & 0 & ... & 0 \end{bmatrix},$$

$$A_0 = \begin{bmatrix} a_{11} - \sum_{j=1}^m b_{1j}\frac{k_j}{2}c_{j1} & ... & a_{1n} - \sum_{j=1}^m b_{1j}\frac{k_j}{2}c_{jn} \\ \vdots & \ddots & \vdots \\ a_{n1} - \sum_{j=1}^m b_{nj}\frac{k_j}{2}c_{j1} & ... & a_{nn} - \sum_{j=1}^m b_{nj}\frac{k_j}{2}c_{jn} \end{bmatrix},$$

$$B_0 = B, \quad C_0 = C, \quad D_0 = 0, \quad E_j = \begin{bmatrix} -\frac{k_j}{2}b_{1j} \\ \vdots \\ -\frac{k_j}{2}b_{nj} \end{bmatrix}, \quad F_j = 0,$$

$$G_j = \begin{bmatrix} c_{j1} \\ \vdots \\ c_{jn} \end{bmatrix}^T, \quad H_j = 0, \quad for \quad j = 1, ..., m.$$

Proof. It can be found in [39]. □

The Theorems 4 and 5 are results that clearly show the relationship of the Lurie problem with LFT-μ-theories in the area of robust control. These theorems were constructed based on the results provided by Lemmas 1 and 2 together with the μ and LFT theories of Doyle, Zhou, and Skogestad.

Theorem 4 ([39])**.** *Let $[0, k_j]$ be the sectors that limit $f_j(\sigma_j)$ such that $f_j \in F_{(0,k_j]}$ for $j = 1, ..., m$, and assume that A_0 is Hurwitz. Then, the system (3.2) is absolutely stable for some class of functions in the sector if*

$$\mu(\Lambda_{22}(j\omega)) < 1, \quad \forall\omega, \tag{4.6}$$

where

$$\Lambda_{22} = C(sI - A_0)^{-1}E,$$

with

$$A_0 = \begin{bmatrix} a_{11} - \sum_{j=1}^{m} b_{1j}\frac{k_j}{2}c_{j1} & \dots & a_{1n} - \sum_{j=1}^{m} b_{1j}\frac{k_j}{2}c_{jn} \\ \vdots & \ddots & \vdots \\ a_{n1} - \sum_{j=1}^{m} b_{nj}\frac{k_j}{2}c_{j1} & \dots & a_{nn} - \sum_{j=1}^{m} b_{nj}\frac{k_j}{2}c_{jn} \end{bmatrix},$$

$$E = \begin{bmatrix} -\frac{k_1}{2}b_{11} & \dots & -\frac{k_m}{2}b_{1m} \\ \vdots & \ddots & \vdots \\ -\frac{k_1}{2}b_{n1} & \dots & -\frac{k_m}{2}b_{nm} \end{bmatrix}.$$

Here, a_{ij}, b_{ij}, and c_{ij} are coefficients of the matrices A, B, and C, respectively.

Proof. It can be found in [39]. □

Theorem 5 ([39])**.** *Let $[\underline{k}_j, \bar{k}_j]$ be the sectors that limit $f_j(\sigma_j)$ such that $f_j \in F_{[\underline{k}_j,\bar{k}_j]}$ for $j = 1, ..., m$, and assume that $\bar{A}_0$ is Hurwitz. Then, the system (3.2) is absolutely stable for some class of functions in the sector, if*

$$\mu(\bar{\Lambda}_{22}(j\omega)) < 1, \quad \forall\omega. \tag{4.7}$$

where

$$\bar{\Lambda}_{22} = C(sI - \bar{A}_0)^{-1}\bar{E},$$

with

$$\bar{A}_0 = \begin{bmatrix} a_{11} - \sum_{j=1}^{m} b_{1j}(\frac{\bar{k}_j+\underline{k}_j}{2})c_{j1} & \dots & a_{1n} - \sum_{j=1}^{m} b_{1j}(\frac{\bar{k}_j+\underline{k}_j}{2})c_{jn} \\ \vdots & \ddots & \vdots \\ a_{n1} - \sum_{j=1}^{m} b_{nj}(\frac{\bar{k}_j+\underline{k}_j}{2})c_{j1} & \dots & a_{nn} - \sum_{j=1}^{m} b_{nj}(\frac{\bar{k}_j+\underline{k}_j}{2})c_{jn} \end{bmatrix},$$

$$\bar{E} = \begin{bmatrix} -(\frac{\bar{k}_1-\underline{k}_1}{2})b_{11} & \dots & -(\frac{\bar{k}_m-\underline{k}_m}{2})b_{1m} \\ \vdots & \ddots & \vdots \\ -(\frac{\bar{k}_1-\underline{k}_1}{2})b_{n1} & \dots & -(\frac{\bar{k}_m-\underline{k}_m}{2})b_{nm} \end{bmatrix}.$$

Here, a_{ij}, b_{ij}, and c_{ij} are coefficients of the matrices A, B, and C, respectively.

Proof. It can be found in [39]. □

The following theorem (presented as conjecture in [39]), a less conservative sufficient condition for the absolute stability of system (3.3) is presented, offering an improvement over other existing theorems. It is an extension of the result of Theorems 4 and 5, where delay is now inserted. The proof of the Theorem 6 was only presented in the doctoral thesis [38]. The same idea was used to prove the main result of [43]. Here, one presents an overview of the proof, which is lengthy. The complete proof can be found in [38] or [43].

Theorem 6. *Suppose that $f_j \in F_{[\underline{k}_j,\bar{k}_j]}$ for $j = 1,...,m$, and assume that $\bar{\Lambda}_{22,delay}$ with the delay term replaced by the Padé approximations of all orders are stable. Then, the system (3.3) is absolutely stable for some class of functions in the sector if*

$$\mu(\bar{\Lambda}_{22,k}(j\omega)) < 1, \quad \forall\omega, \forall k \in \mathbb{Z}^+, \tag{4.8}$$

where

$$\bar{\Lambda}_{22,delay} = C(sI - \bar{A}_0 - F_\tau e^{-\tau s})^{-1}\bar{E},$$

$$\bar{\Lambda}_{22,k}(j\omega) = C(j\omega I - \bar{A}_0 - F_\tau[k/k])^{-1}\bar{E},$$

with

$$\bar{A}_0 = \begin{bmatrix} a_{11} - \sum_{j=1}^m b_{1j}(\frac{\bar{k}_j+\underline{k}_j}{2})c_{j1} & ... & a_{1n} - \sum_{j=1}^m b_{1j}(\frac{\bar{k}_j+\underline{k}_j}{2})c_{jn} \\ \vdots & \ddots & \vdots \\ a_{n1} - \sum_{j=1}^m b_{nj}(\frac{\bar{k}_j+\underline{k}_j}{2})c_{j1} & ... & a_{nn} - \sum_{j=1}^m b_{nj}(\frac{\bar{k}_j+\underline{k}_j}{2})c_{jn} \end{bmatrix},$$

$$\bar{E} = \begin{bmatrix} -(\frac{\bar{k}_1-\underline{k}_1}{2})b_{11} & ... & -(\frac{\bar{k}_m-\underline{k}_m}{2})b_{1m} \\ \vdots & \ddots & \vdots \\ -(\frac{\bar{k}_1-\underline{k}_1}{2})b_{n1} & ... & -(\frac{\bar{k}_m-\underline{k}_m}{2})b_{nm} \end{bmatrix}.$$

Here, $[k/k]$ is the Padé approximation of denominator and numerator degrees equal to k, and a_{ij}, b_{ij}, and c_{ij} are coefficients of the matrices A, B, and C, respectively.

Proof. Theorem 6 is an extension of the Theorem 5, where the delay is inserted. First, transform the system (3.3), without delay, into (4.1). Next, by applying Lemma 2, one has:

$$\begin{cases} \dot{x} = & \bar{A}_0x+ & \bar{B}_0r_1+ & \bar{E}p, \\ \sigma = & \bar{C}_0x+ & \bar{D}_0r_1+ & \bar{F}p, \\ q = & \bar{G}x+ & \bar{H}r_1. & \end{cases} \tag{4.9}$$

By introducing the delay, one obtains

$$\begin{cases} \dot{x} = & \bar{A}_0x+ & \bar{B}_0r_1+ & \bar{E}p+ & F_\tau x(t-\tau), \\ \sigma = & \bar{C}_0x+ & \bar{D}_0r_1+ & \bar{F}p, & \\ q = & \bar{G}x+ & \bar{H}r_1. & & \end{cases} \tag{4.10}$$

By applying the Laplace transform, the following is obtained:

$$\begin{cases} sX(s) = & \bar{A}_0X(s)+ & \bar{B}_0r_1(s)+ & \bar{E}p(s)+ & F_\tau e^{-\tau s}X(s), \\ \sigma(s) = & \bar{C}_0X(s)+ & \bar{D}_0r_1(s)+ & \bar{F}p(s), & \\ q(s) = & \bar{G}X(s)+ & \bar{H}r_1(s). & & \end{cases} \tag{4.11}$$

Starting with the initial equation of (4.11), one has:

$$X(s) = (sI - \bar{A}_0 - F_\tau e^{-\tau s})^{-1}\bar{B}_0r_1(s) + (sI - \bar{A}_0 - F_\tau e^{-\tau s})^{-1}Ep(s).$$

Inserting $X(s)$ in the 2nd and 3rd equation of (4.11), one gets:

$$\sigma(s) = [\bar{C}_0(sI - \bar{A}_0 - F_\tau e^{-\tau s})^{-1}\bar{B}_0 + \bar{D}_0]r_1(s) + [\bar{C}_0(sI - \bar{A}_0 - F_\tau e^{-\tau s})^{-1}\bar{E} + \bar{F}]p(s)$$

and

$$q(s) = [\bar{G}(sI - \bar{A}_0 - F_\tau e^{-\tau s})^{-1}\bar{B}_0 + \bar{H}]r_1(s) + \bar{G}(sI - \bar{A}_0 - F_\tau e^{-\tau s})^{-1}\bar{E}p(s).$$

As a result, the LFT is derived with the inputs $[r_1\ p]^T$ and outputs $[\sigma\ q]^T$:

$$\begin{bmatrix} \sigma \\ q \end{bmatrix} = \begin{bmatrix} \bar{C}_0(sI - \bar{A}_0 - F_\tau e^{-\tau s})^{-1}\bar{B}_0 + \bar{D}_0 & \bar{C}_0(sI - \bar{A}_0 - F_\tau e^{-\tau s})^{-1}\bar{E} + \bar{F} \\ \bar{G}(sI - \bar{A}_0 - F_\tau e^{-\tau s})^{-1}\bar{B}_0 + \bar{H} & \bar{G}(sI - \bar{A}_0 - F_\tau e^{-\tau s})^{-1}\bar{E} \end{bmatrix} \begin{bmatrix} r_1 \\ p \end{bmatrix}. \tag{4.12}$$

From (4.12) and $\bar{G} = C$ (Lemma 2), one has $\bar{\Lambda}_{delay}$

$$\begin{aligned} \bar{\Lambda}_{delay} &= \begin{bmatrix} \bar{\Lambda}_{11,delay}(s) & \bar{\Lambda}_{12,delay}(s) \\ \bar{\Lambda}_{21,delay}(s) & \bar{\Lambda}_{22,delay}(s) \end{bmatrix} \\ &= \begin{bmatrix} \bar{C}_0(sI - \bar{A}_0 - F_\tau e^{-\tau s})^{-1}\bar{B}_0 + \bar{D}_0 & \bar{C}_0(sI - \bar{A}_0 - F_\tau e^{-\tau s})^{-1}\bar{E} + \bar{F} \\ C(sI - \bar{A}_0 - F_\tau e^{-\tau s})^{-1}\bar{B}_0 + \bar{H} & C(sI - \bar{A}_0 - F_\tau e^{-\tau s})^{-1}\bar{E} \end{bmatrix}. \end{aligned} \tag{4.13}$$

As shown in [39], it is enough to analyze $\bar{\Lambda}_{22,delay}(s)$ under the criterion of μ-analysis (see Theorem 4 in [39]) to gather details about the system's stability in study. So, from now on, one inserts the Padé approximations represented by $[k/k]$. When the exponential is replaced by a Padé approximation, one obtains a sequence of rational matrices, which are represented by:

$$\bar{\Lambda}_{22,k}(j\omega) = C(j\omega I - \bar{A}_0 - F_\tau[k/k])^{-1}\bar{E}. \tag{4.14}$$

In the limit, a matrix is obtained that contains an infinite number of poles and zeros. For each k in this sequence of matrices, one has a sequence of SSV functions:

$$\mu_k(j\omega) = \mu_\Delta(\bar{\Lambda}_{22,k}(j\omega)), \tag{4.15}$$

where the matrix Δ is diagonal, representing the uncertainty structure associated with the Lurie problem.

The rest of the proof consists of verifying that the sequence of functions (4.15) converges. The proof that this sequence converges can be found in [38, pp. 116–120] or [43, proof of Theorem 4]. □

Next, a theorem is presented that allows the synthesis of controllers, and which can be used in conjunction with DK-iteration (see Algorithm 1 of [39]). This theorem is due to [39] and direct applications of this theorem are made in the medical field (see [3,38]).

Theorem 7 ([39])**.** *Given a controller $K(s)$ and $[0, k_j]$, the sectors that include $f_j \in F_{(0,k_j]}$ for $j = 1, ..., m$, then the system (4.1) with the controller $K(s)$ in the feedback loop is robustly stable and has the robustness of performance if, and only if,*

$$\mu_{\tilde{\Delta}}\left(\begin{bmatrix} M_{11}(j\omega) & M_{12}(j\omega) \\ M_{21}(j\omega) & M_{22}(j\omega) \end{bmatrix}\right) < 1, \quad \forall\omega, \tag{4.16}$$

where

$$M_{11}(s) = I + C(sI - A_0)^{-1}BK(s)(-I)[I + C(sI - A_0)^{-1}BK(s)]^{-1},$$

$$M_{12} = C(sI - A_0)^{-1}E + C(sI - A_0)^{-1}BK(s)(-C)(sI - A_0)^{-1}E[I + C(sI - A_0)^{-1}BK(s)]^{-1},$$

$$M_{21} = C(sI - A_0)^{-1}E + C(sI - A_0)^{-1}BK(s)(-I)[I + C(sI - A_0)^{-1}BK(s)]^{-1},$$

$$M_{22} = C(sI - A_0)^{-1}E + C(sI - A_0)^{-1}BK(s) - C(sI - A_0)^{-1}E[I + C(sI - A_0)^{-1}BK(s)]^{-1},$$

with

$$A_0 = \begin{bmatrix} a_{11} - \sum_{j=1}^{m} b_{1j}\frac{k_j}{2}c_{j1} & \dots & a_{1n} - \sum_{j=1}^{m} b_{1j}\frac{k_j}{2}c_{jn} \\ \vdots & \ddots & \vdots \\ a_{n1} - \sum_{j=1}^{m} b_{nj}\frac{k_j}{2}c_{j1} & \dots & a_{nn} - \sum_{j=1}^{m} b_{nj}\frac{k_j}{2}c_{jn} \end{bmatrix},$$

$$E = \begin{bmatrix} -\frac{k_1}{2}b_{11} & \dots & -\frac{k_m}{2}b_{1m} \\ \vdots & \ddots & \vdots \\ -\frac{k_1}{2}b_{n1} & \dots & -\frac{k_m}{2}b_{nm} \end{bmatrix}.$$

Proof. It can be found in [39]. □

5. Review on medical and biological applications

In recent years, the Lurie problem has received significant attention in the field of medical and biological applications. This section aims to provide a comprehensive overview of how the Lurie problem plays out in contemporary biomedical understanding and innovation. There are certainly many problems in the literature that have a Lurie-type system in their models used in medical and biological areas, but which have not been presented as a Lurie-type system by the authors. However, this review basically looked for articles that had the terms "absolute stability" or "Lurie-type systems" in their text. According to the methods presented in Section 2, the Table 3 shows the studies found in this review, relating the medical and biological areas to the respective works. Following this section, some of these works will be presented in more detail with some discussion of their relationship to the Lurie problem and proposals for future research.

5.1. Anesthesiology

In the field of anesthesiology, this review identified the paper [59], which investigated robust stability under nonlinear uncertainty using a linear pharmacokinetics and nonlinear pharmacodynamics (PKPD) model and a proportional-integral-derivative (PID) controller. The complete system was formulated as a Lurie problem. The study employed the circle criterion to establish stability boundaries, demonstrating their adequacy in managing inter-individual variability in nonlinearity.

Figure 8 shows the complete block diagram of the system with sector nonlinearity. In addition, a controller is inserted into this system in order to stabilize it. From this system, the authors obtain their mathematical model, and then rearrange this model to place it in the form of a Lurie-type system of the SISO case [59]:

$$\begin{cases} \dot{z} = Az + Bq, \\ C_e = Cz + Dq, \\ E = \phi(C_e), \end{cases} \tag{5.1}$$

where

$$A = \begin{bmatrix} A_p & B_pC_c \\ 0 & A_c \end{bmatrix}, \ B = \begin{bmatrix} -B_pD_c \\ -B_c \end{bmatrix},$$

$$C = [C_p \quad D_pC_c], \ D = [-D_pD_c] \ and \ q = E \ or \ w.$$

Subsequently, a PID controller was obtained via the *sisotool* tuning method in MATLAB. Finally, the system's robustness was analyzed using the circle criterion.

In this work, although a controller was obtained, the issue of performance robustness was not well-evaluated. Furthermore, the circle criterion is the most basic stability criterion for the Lurie problem, which provides very conservative conditions. Therefore, this is an interesting problem to apply Popov's criterion (Theorem 2) or more recent theorems for the Lurie problem, such as those presented by the Theorems 5 and 7. Note that in order to use these two theorems in their current form, the direct transmission matrix (D) must be incorporated into the system, where a simple transformation of augmented states in (5.1) is enough.

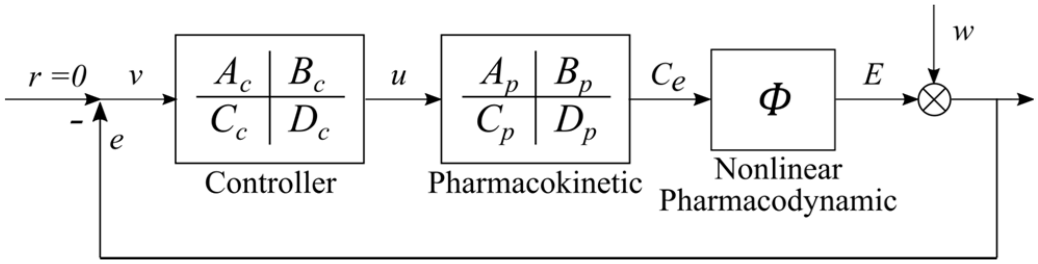


Figure 8. Anesthesia control system. Adapted from Ref. [59].

Table 3. Table relating works on applications of the Lurie problem to the respective medical and biological areas.

Area	Works	Specific examples
Anesthesiology	Anesthesia system with nonlinear uncertainty [59]	Chang and Syafiie [59] addressed robust stability in a linear and nonlinear PKPD model, formulating the system as a SISO Lurie problem without delay, similar to Eq (3.1). It used the circle criterion to define stability bounds, but the assessment of robustness performance was limited. The work suggests that more advanced criteria, such as Popov's, could improve the analysis of the system's robustness.
Cardiology	Models of cardiac mechanics [60]	The paper [60] examines how numerical oscillations arise in cardiac models due to the influence of fiber shortening velocity on generation of force. It evaluates the stability of a mathematical model combining ODEs and partial differential equations (PDE) for cardiac mechanics. This work may have a link to Lurie's absolute stability, which merits further exploration. Depending on the problem to be modeled, the Lurie-type system could take the form similar to the SISO or MIMO cases with or without delay.
Endocrinology	Analysis of mathematical models of diabetes [61]	The paper [61] deals with the absolute stability of a type 1 diabetes model with delay (Lurie-type MIMO system with delay similar to Eq (3.3)). In this work, most stability studies use a linearized system.
Epidemiology	Analysis of a delayed susceptible-infected-recovered (SIR) model [62]; model of malaria with immune delay [63]; analysis of absolute stability and Hopf bifurcation in malaria model [64]; SIR model with general nonlinear [65]; population dynamics [66]	Liu [65] examines a lagged SIR model with a non-linear rate of incidence and logistic growth of susceptible, modeled as a Lurie-type SISO system with delay. The incidence function $F(S)$ is continuous, strictly increasing, and treated as a sectorial nonlinearity.
General medical devices	Micro-manipulator for medical application [67]; mechanical ventilation [68, 69]; patient-robot-therapist [70]; robot in telesurgery [71]; fluid resuscitation [72]; actuator for nanobiomedicine [73]	In [69], a repetitive control design for Lurie-type SISO systems without delay (as Eq (3.1)) is applied to mechanical ventilation in intensive care unit, ensuring stable target pressure profile tracking.
Neuroscience	Neural networks and memory model [4, 53, 74–83]; Parkinson's disease [84]; Alzheimer's disease [2, 3, 38]; neural mass models to simulate electroencephalography (EEG) signals [85–87]	In [2], a simple model of Alzheimer-like disease (ALD) without delay is derived from a Hopfield neural network (HNN) that serves to model memory degradation. The pathology is controlled using a controller designed from Lurie-type control system theories (Theorem 7), effectively curating the computational model. In this model, one has a Lurie-type MIMO system without delay, similar to Eq (3.2).
Oncology	Dynamics in leukemia [88]; model of tumor-immune interaction [89]; Chaos and optimal control of tumor system with drug [90]	In [88], the cellular dynamics of acute myeloblastic leukemia are analyzed to establish stability conditions for effective drug delivery. The model under analysis can be considered a Lurie-type SISO system with delay, and the Popov, circle, and nonlinear small gain criteria are applied to study stability, extending previous results on local asymptotic stability.

5.2. Cardiology

In the paper [60], the issue of numerical oscillations in velocity-dependent active cardiac models, caused by the dependence of fiber shortening velocity for force generation, is addressed. The work starts from a mathematical model of active force generation formulated as a system of ODEs, coupled with a model describing cardiac mechanics via PDE. Focusing on the ODE model, the system (5.2) is a possible candidate for transformation into a Lurie-type system:

$$\begin{cases} \dot{r}(t) = h(r(t), [Ca_i^{2+}(t), \lambda(t), \dot{\lambda}(t)]), \\ T_a(t) = g(r(t)), \\ r(0) = r_0, \end{cases} \tag{5.2}$$

where $r(t)$ is the vector of state variables (protein concentration), the model input is Ca, and λ tissue strain in the fibers direction. The output T is the tension generated by the muscles, and the functions h and g can be nonlinearities of the model in question.

Following this, the models are discretized (the same can be done with Lurie-type systems; see [42]), initiating a stability analysis of the numerical method. Initially, this work can be viewed in terms of using the terminology of absolute stability, albeit not directly related to the Lurie problem. However, certain propositions in this work suggest a potential connection to the study of the Lurie absolute stability. Future investigation of this work would be valuable to gain insights and explore its relationships with the Lurie problem, if any exist. A starting point is the establishment of the model in Eq (5.2) as a Lurie-type system.

5.3. Endocrinology

In the field of endocrinology, research has been conducted that examines the absolute stability of a model related to type 1 diabetes [61]. The paper [61] investigates the stability of a mathematical model of type 1 diabetes due to [91]. The model is represented by the system (5.3)

$$\begin{cases} \dot{x}(t) = f_1(\frac{0.1z(t)}{V_3}) - (\frac{E}{V_1} + \frac{1}{T_1})x(t) + \frac{E}{V_2}y(t), \\ \dot{y}(t) = \frac{E}{V_1}x(t) - (\frac{E}{V_2} + \frac{1}{T_2})y(t), \\ \dot{z}(t) = f_3(\frac{x(t-T)}{V_1}) - \frac{0.1z(t)}{V_3}f_2(\frac{y(t)}{V_2}) + (L - p_0), \end{cases} \tag{5.3}$$

where $E, V_1, V_2, V_3, T_1, T_2$ are real constants inherent to the model, and the functions f_i are restricted to the first and third quadrants of the plane. In addition, the model has the delay $x(t - T)$, which makes it similar to a Lurie-type system with delay (see Eq (3.3)). From the analyses performed, the authors obtain conclusions about the absolute stability of the system (5.3). In relation to this study, some observations can be made:

1) The majority of stability studies are based on the linearized form of the system (5.3).

2) According to Lemma 1 of [61], a necessary and sufficient condition for absolute stability is provided. However, when considering absolute stability, the linearized system should not be used, but rather the system with its nonlinearities.

3) For a more accurate analysis of the absolute stability of the system (5.3), a theorem that analyzes a Lurie-type system with delay should be used.

Therefore, an interesting suggestion for future work could be to analyze the stability of the system [61] using the ideas of the Theorem 6. To this end, a small extension of this theorem could be created, taking into account delays inside of nonlinearities.

5.4. Epidemiology

Studies on absolute stability cover some models in epidemiology and population dynamics. In [62], the authors examined a delayed SIR model – where the numbers of susceptible, infected, and recovered individuals at time t are considered – with a nonlinear incidence rate. They demonstrated that the global dynamics of the disease depend on the threshold value and incubation time, which influence whether the disease persists or dies out. By using the time delay as a bifurcation parameter, they explored the local stability of the endemic equilibrium and derived conditions for the system to be either absolutely stable or conditionally stable. Building on this, [65] investigated a SIR epidemic model that includes a delay in incubation time and an overall nonlinear incidence rate, with the increase in susceptible subjects regulated by the logistic equation. In [63, 64], the authors investigated the disease-free equilibrium in mathematical models of intra-host dynamics for plasmodium falciparum malaria, and the papers contradict themselves in some of their findings on absolute stability and Hopf bifurcations. Franco et al. [66] explored population dynamics through forced difference equations, establishing conditions for boundedness and persistence in ecological models, emphasizing stability despite external disturbances. These works collectively contribute to the understanding of absolute stability of complex biological systems.

More specifically, taking as an example the study of [65] on a SIR model, one has in Eq (5.4) a Lurie-type system with delay

$$\begin{cases} \dot{S}(t) = rS(t)(1 - \frac{S(t)}{K}) - \beta F(S(t))I(t-\tau), \\ \dot{I}(t) = \beta F(S(t))I(t-\tau) - (\mu_1 + \gamma)I(t), \\ \dot{R}(t) = \gamma I(t) - \mu_2 R(t). \end{cases} \tag{5.4}$$

It should be noted that F is continuous on $[0, +\infty)$ and continuously differentiable on $(0, \infty)$. Furthermore, it is assumed that $F(s)$ is strictly monotonically increasing on $[0, +\infty)$ with $F(0) = 0$. In these terms, $F(S)$ fits as a sectorial nonlinearity in the plane, and the system can therefore be approached as a Lurie-type system. In this case, [65] extends the model of [62], and the study is carried out in a way that provides important conclusions about the absolute stability of the system (5.4). However, it should be noted that the work only employs the theory of asymptotic autonomous systems to analyze the absolute stability of the system (5.4). Therefore, as in the case of diabetes, it would be interesting to analyze this problem using specific results from the theory of absolute stability for Lurie-type systems with delay (Theorem 6).

5.5. Medical devices

The review explores the application of Lurie-type systems and absolute stability concepts in medical devices, highlighting several studies. In [67], a servo-controlled micro-manipulator for medical applications uses a feedback loop model with an asymptotically stable linear part (the manipulator) and a nonlinear time-dependent part (the operator's finger), employing the circle criterion to confirm stability. Similarly, Hohenhaus et al. [72] applies the circle criterion to ensure stability in a robust closed-loop control strategy for fluid resuscitation using observer-based techniques. In the context of mechanical ventilation, the system is modeled as a Lurie-type system, combining linear time-invariant dynamics with static nonlinearity. Reinders et al. [69] demonstrates a repetitive control design with stability guarantees for mechanical ventilation, while Shakib et al. [68] presents a parametric identification method for continuous-time Lurie-type systems. Delving into [69], the system is modeled as an SISO Lurie-type system described by the equation:

$$\begin{cases} \dot{x} = Ax + Bu + Ew, \\ y = Mx + Nw, \\ w = -\phi(y), \\ v = Cx + Dw. \end{cases} \tag{5.5}$$

In [69], the repetitive control method is applied to a nonlinear ventilation system for the intensive care unit, based on Lurie-type system (Eq (5.5)). The experimental results confirm that the RC scheme successfully tracks the desired target pressure profile, providing adequate ventilation support for adult patients. This work introduces a transformation of the mechanical ventilation system into a Lurie-type system, beginning with the derivation of individual models for the plant components: the blower model G_b (5.6), the hose model R_{hose} (5.7), and the patient-leak model G_p (5.8). These models are subsequently merged to form an open-loop Lurie-type system, facilitating controller design and stability evaluation. The blower model G_b is obtained through sixth-order fitting based on frequency response measurements of the blower's actual dynamics:

$$\begin{cases} \dot{x}_b = A_b x_b + B_b p_c, \\ p_{\text{out}} = C_b x_b. \end{cases} \tag{5.6}$$

Using experimental data and the relation between the flow rate through the Q_{out} hose and the pressure difference across the hose ($\Delta p := p_{out} - p_{aw}$), the hose is represented in the following manner (where R_1 and R_2 are the hose-resistance parameters):

$$Q_{\text{out}} := R_{\text{hose}}(\Delta p) = \text{sign}(\Delta p) \frac{-R_1 + \sqrt{R_1^2 + 4R_2|\Delta p|}}{2R_2}. \tag{5.7}$$

Subsequently, the integrated patient-leak model G_p defines the relationship between the outlet flow Q_{out} and the output of the system $y = p_{aw}$. This model for the patient is represented by the following first-order state-space representation (see a_p, b_p, and c_p in [69]):

$$\begin{cases} \dot{p}_{\text{lung}} = a_p p_{\text{lung}} + b_p Q_{\text{out}}, \\ p_{\text{aw}} = c_p p_{\text{lung}} + d_p Q_{\text{out}}. \end{cases} \tag{5.8}$$

Finally, by combining the blower, the hose, and the patient model, one has an open circuit model of p_c to p_{aw} in the form of (5.5), where

$$A = \begin{bmatrix} A_b & 0 \\ -(1-\eta d_p)^{-1}\eta C_b b_p & a_p + \eta c_p(1-\eta d_p)^{-1} b_p \end{bmatrix}, \quad B = \begin{bmatrix} B_b \\ 0 \end{bmatrix},$$

$$E = \begin{bmatrix} 0 \\ -b_p(1-\eta d_p)^{-1} \end{bmatrix}, \quad M = \begin{bmatrix} C_b + d_p(1-\eta d_p)^{-1}\eta C_b \\ -c_p - d_p(1-\eta d_p)^{-1}\eta c_p \end{bmatrix}^T,$$

$$N = d_p(1-\eta d_p)^{-1}, D_o = -d_p(1-\eta d_p)^{-1},$$

$$C = \left[-d_p(1 - \eta d_p)^{-1}\eta C_b \quad c_p + d_p(1 - \eta d_p)^{-1}\eta c_p \right].$$

To ensure that the linear dynamics of the open-loop plant in Lurie-type form are controllable and observable, the term $\eta\Delta p$ is added to the nonlinear resistance of the hose, i.e., making the nonlinearity as follows:

$$\varphi(y) := R_{\text{hose}}(y) + \eta y.$$

Some other studies using the terminology of absolute stability in medical devices have been found. In [70], a bilateral impedance control strategy for delayed tele-robotic systems used in patient-therapist collaboration is proposed, proving stability by means of the criterion of absolute stability. Similarly, Souzanchi-K and Akbarzadeh-T [71] introduces brain emotional learning for tele-surgical robots to manage uncertainties and balance transparency with stability, using Lyapunov theory and presenting Llewellyn's criterion to establish absolute stability conditions. While these works use the term "absolute stability", further investigation is needed to determine their connection to the Lurie problem. In [73], the absolute stability conditions for control systems with electro magneto elastic actuators in nano-biomedicine are analyzed using frequency methods and Lyapunov's criterion. The Yankelovich criterion, extending Popov's criterion, is applied to account for the hysteresis nonlinearity of the actuators, simplifying the system's stability analysis.

5.6. Neuroscience

Neuroscience, a multidisciplinary field, has significant medical implications, particularly in diagnosing and treating neurological disorders. The references are grouped into three categories: the first focuses on Lurie-type systems or absolute stability theory applied to artificial neural network (ANN) for memory modeling, the second addresses the application of the Lurie problem to Alzheimer's and Parkinson's diseases, and the third explores the use of Lurie-type systems to generate signals simulating EEG.

5.6.1. The Lurie problem applied to ANNs

The concept of absolute stability has been widely applied to neural networks and complex systems, with early work such as [78] leading to further studies on Hopfield's neural networks, including [4, 39, 74, 75, 83, 92]. Advances have been made in stability analysis and control design, particularly using robust control theory and DK-Iteration. Discrete-time recurrent neural networks (RNNs) have been studied for global Lyapunov stability through LMI [79, 80], while neural field models have been analyzed for absolute stability and synchronization [81,82], illustrating the relevance of absolute stability in neuroscience and control systems.

The literature has shown [4, 83] that there are important relationships between the Lurie problem and HNN [93]. HNN can be described by this set of nonlinear ODEs:

$$C_i \frac{du_i}{dt} = -\frac{u_i}{R_i} + \sum_{j=1}^{n} T_{ij} V_j + I_i, \qquad i = 1, 2, ..., n, \tag{5.9}$$

where $C \in \mathbb{R}^n$, $u \in \mathbb{R}^n$, $R \in \mathbb{R}^n$, $T \in \mathbb{R}^{nxn}$, $I \in \mathbb{R}^n$, and $V_j = g(u_i)$. The nonlinear function g can be defined as $g : \mathbb{R} \to [0, 1]$, is differentiable without interruption and increases in a monotonic manner, or $g_i'(u_i) > 0$. One can note from the nonlinearity that this fits into a MIMO Lurie-type system. In [39], new sufficient conditions for absolute stability and controller synthesis techniques are proposed for HNN based on the theory of Lurie-type systems. The following provides a detailed transformation of Eq (5.9) into a Lurie-type system, demonstrating that the HNN is, in fact, a specific case of the Lurie-type system given in (3.2).

To start, considering the conditions mentioned for the function g, it can be assumed that it is a part of the class of functions F_∞ of Lurie problem:

$$g \in F_\infty := \{g | g(0) = 0, u_i g(u_i) > 0, g \neq 0\}.$$

Then, passing C_i and dividing to the right side of (5.9), new constants are defined: $d_i = \frac{1}{C_i R_i}$, $b_{ij} = \frac{T_{ij}}{C_i}$, $U_i = \frac{I_i}{C_i}$, and the HNN becomes

$$\frac{du_i}{dt} = -d_i u_i + \sum_{j=1}^{n} b_{ij} g_j(u_j) + U_i. \tag{5.10}$$

To eliminate the external input U_i, the following transformation is made: $u_i = y_i + \frac{U_i}{d_i}$ and $G_i(y_i) = g_i(y_i + \frac{U_i}{d_i})$. Since $y_i = u_i - \frac{U_i}{d_i}$, so $\frac{dy_i}{dt} = \frac{du_i}{dt}$; thus, substituting in (5.10), one has

$$\frac{dy_i}{dt} = -d_i(y_i + \frac{U_i}{d_i}) + \sum_{j=1}^{n} b_{ij} G_j(y_j) + U_i \quad \rightarrow \quad \frac{dy_i}{dt} = -d_i y_i - U_i + \sum_{j=1}^{n} b_{ij} G_j(y_j) + U_i,$$

$$\frac{dy_i}{dt} = -d_i y_i + \sum_{j=1}^{n} b_{ij} G_j(y_j). \tag{5.11}$$

Therefore, using this transformation, the input U_i of HNN becomes zero, as shown in (5.11).

The goal is to understand how solutions behave near the equilibrium point, so to find the equilibrium point for the system (5.11), one does

$$-d_i y_i + \sum_{j=1}^{n} b_{ij} G_j(y_j) = 0.$$

In general, for the Lurie problem, the equilibrium point of interest is assumed to be located at the origin of R^n, but from (5.11), if this is not the case, a translation can be made using a suitable change of variables. So, let $y = [y_1, y_2, ..., y_n]^t \in R^n$ and suppose that $y = y^* \neq 0$ is an equilibrium point of interest from (5.11). For $i = 1, 2, ..., n$, the appropriate change of variables to translate the equilibrium point to the origin is

$$\tilde{x}_i = y_i - y_i^*, \text{ and } f(\tilde{x}_i) = G(y_i) - G(y_i^*) = G(\tilde{x}_i + y_i^*) - G(y_i^*).$$

Since $y_i = x_i + y_i^* \rightarrow \frac{dy_i}{dt} = \frac{d\tilde{x}_i}{dt}$ and $G(y_i) = f(\tilde{x}_i) + G(y_i^*)$, substituting in (5.11), one gets:

$$\frac{d\tilde{x}_i}{dt} = -d_i(\tilde{x}_i + y_i^*) + \sum_{j=1}^{n} b_{ij}[f_j(\tilde{x}_j) + G_j(y_j^*)] = -d_i\tilde{x}_i - d_i y_i^* + \sum_{j=1}^{n} b_{ij} f_j(\tilde{x}_j) + \sum_{j=1}^{n} b_{ij} G_j(y_j^*),$$

$$\frac{d\tilde{x}_i}{dt} = -d_i\tilde{x}_i + \sum_{j=1}^{n} b_{ij} f_j(\tilde{x}_j) + \{-d_i y_i^* + \sum_{j=1}^{n} b_{ij} G_j(y_j^*)\}.$$

Note that by the definition of the equilibrium point, the expression inside the braces is zero. Therefore, the HNN presented in (5.9) becomes:

$$\frac{d\tilde{x}_i}{dt} = -d_i\tilde{x}_i + \sum_{j=1}^{n} b_{ij} f_j(\tilde{x}_j). \tag{5.12}$$

In relation to the function f, one has:

$$f_i(\tilde{x}_i) = G(\tilde{x}_i + y_i^*) - G(y_i^*) \to f_i(0) = G(y_i^*) - G(y_i^*) = 0 \quad \text{and} \quad f_i' = g_i' > 0 \quad (i = 1, 2, ..., n),$$

so, with f continuous, one has:

$$f \in F_\infty := \{f | f(0) = 0, \quad x_i f(\tilde{x}_i) > 0, \quad \tilde{x}_i \neq 0\}.$$

Returning to the Eq (3.2) of the Lurie problem:

$$\begin{cases} \dot{x} = Ax - Bf(\sigma) + Br_1, \\ \sigma = Cx, \end{cases}$$

it can be assumed, without loss of generality, that the set of line vectors $c_i = (c_{i1}, ..., c_{in})$, $i = 1, 2, ..., m$ of matrix C is linearly independent and a transformation is used to separate the variables (see [4]), so the system (3.2) can be converted in (5.13):

$$\dot{\tilde{y}} = \sum_{j=1}^{n} \tilde{a}_{ij}\tilde{y}_j + \sum_{j=n-m+1}^{n} \tilde{b}_j \tilde{f}_j(\tilde{y}_j). \tag{5.13}$$

Comparing Eq (5.12) with Eq (5.13), one can see that HNN is a special case of a MIMO Lurie-type system, where $\tilde{a}_{ij} = 0$, $i \neq j$, $\tilde{a}_{ii} = d_i < 0$, and $m = n$.

5.6.2. The Lurie problem applied to Alzheimer's and Parkinson's disease

Recent studies have applied the Lurie problem to model neurological disorders and oscillatory behaviors in biological systems. In [84], cortex-basal ganglia network models with distributed delays are analyzed to explore Hopf bifurcation mechanisms in Parkinson's disease, showing how delays and feedback affect oscillations and stability. Similarly, [2, 3, 38] link HNN and the Lurie problem to Alzheimer's disease, modeling memory degeneration and proposing robust control solutions using DK-iteration. In [2], the Alzheimer-like disease model (ALD) is derived from an HNN model (5.9) and corrected through control strategies based on Theorems 4 and 7, as HNN is shown to be a particular case of the Lurie problem. Moreover, in [3] this model is improved by inserting the delay according to Eq (5.14):

$$\dot{u}_i(t) = -d_i u_i(t) + \alpha T_{i,n-(i-1)} \tanh[u_{n-(i-1)}(t)] + \beta F_{i,i} u_{n-(i-1)}(t-\tau) + I_i. \tag{5.14}$$

Here $u \in \mathbb{R}^n$, $d = diag[1, ..., 1]_{n\times n}$, $T \in S\mathbb{R}^{n\times n}$ is a symmetric matrix, $F = diag[1, ..., 1]_{n\times n}$, $\alpha, \beta, \tau \in \mathbb{R}$, and $I \in \mathbb{R}^n$. Equation (5.14) represents a MIMO Lurie-type system with delay, where the nonlinearity is modeled by a hyperbolic tangent function, fitting the Lurie problem framework. This model, called improved Alzheimer-like disease (IALD), also applied in [43], incorporates delay to better simulate biological neural networks and model varying degrees of memory deterioration. Theorems 6 and 7 are used to correct memory failures. Figure 9, from [3], illustrates this process, showing the network's failure to remember the letter L in Figure 9a and the correction achieved with a controller in Figure 9b.

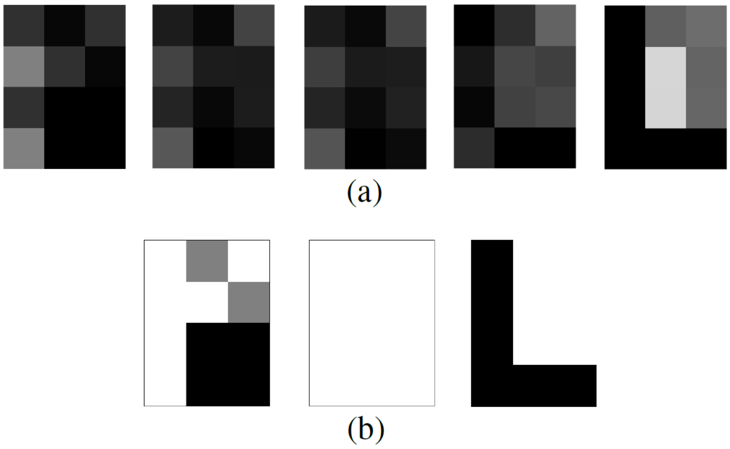


Figure 9. IALD model: (a) IALD with memory fail; (b) IALD healed, i.e., with controller. Adapted from Ref. [3].

5.6.3. The Lurie problem for EEG signals generation

A series of studies have explored the design of robust nonlinear observers for neural mass models using Lurie system theory. Liu et al. [85] introduces a robust nonlinear observer that handles input uncertainty and measurement noise for estimating unmeasured membrane potentials from EEG signals. Similarly, Liu et al. [86] transforms neural mass models into Lurie-type systems to ensure error convergence through numerical simulations, while [87] designs a state observer for neural population models using input-output stability and Lurie theory. In [86], the authors improve observer design by modeling a neural mass system with eight first-order differential equations and sigmoid nonlinearities, reformulating it into a Lurie-type system as shown in (5.15):

$$\begin{cases} \dot{x} = Ax - Bf(Hx) + B_1 u, \\ \sigma = Cx + Dw. \end{cases} \tag{5.15}$$

The design of state observers is of great importance for the mathematical modeling of EEG signals, which provides a powerful tool for analyzing the mechanism of neurological diseases. The main problem in observer design is to ensure convergence of the estimation error and to make it as small as possible. In this approach, future work could investigate the use of new absolute stability theory techniques (for example, the application of Theorems 4–6 and/or the creation of extensions of these) in the search for more efficient observers.

5.7. *Oncology*

In the literature review, some interesting works were found in the oncology area that utilize the theory of absolute stability in some way. El-Gohary [90] focuses on chaos and optimal control of tumor systems, with and without drug intervention, exploring stability and determining optimal dosages to control tumor growth while minimizing the Hamilton function. Özbay et al. [88] analyzes acute myeloblastic leukemia dynamics, applying circle, Popov, and small gain criteria to enhance the stability conditions for drug delivery systems. Chen et al. [89] examines a tumor-immune interaction model with antigen stimulation delay, revealing how delays affect stability and bifurcation behaviors. These studies highlight the potential of absolute stability and Lurie system theories in optimizing cancer treatment, particularly in chemotherapy dosage optimization to balance effectiveness and avoid excessive drug use.

6. Conclusions

The review described in this paper provides a more detailed overview and unprecedented analysis of the Lurie problem (also known as absolute stability theory) and its wide-ranging applications in the medical and biological fields. This comprehensive approach not only highlights the current state of research, but also opens up space for new reflections and recommendations for future researches. Based on this overview, the following sections will present the main conclusions for each case, as well as suggestions for future research.

6.1. *Review of the Lurie problem*

By representing the Lurie problem with a simpler and more comprehensive approach, the paper facilitates a deeper understanding of the basic concepts of stability, including the Aizerman conjecture, and establishes this conjecture as a specific instance of the Lurie problem. Additionally, the link between the Lurie problem and robust control theory is clarified especially by the contributions of Doyle, Skogestad, and Zhou, and this work emphasizes the advancement of new necessary and sufficient conditions for the Lurie problem, as demonstrated by the findings in Section 4. This link underlines the mutual reinforcement between these two areas of study, providing a solid foundation for further advances in control and modeling. In this case, one can expand the theory presented in Section 4 to more general cases of Lurie-type systems, for example, with more types of delay and time-varying parameters. In addition, one can expand the theory to the discrete-time domain, for example, following on from what was done in [42].

An interesting point observed in this work is that the term "absolute stability" has been used in some works as a synonym for the problem of global asymptotic stability for any type of system (e.g., [45, pp. 160]). However, it is important not to disregard the origin of the concept of absolute stability, which stems from the Lurie problem (the books of Khalil [56] and Slotine [57] deal carefully with the concept of absolute stability). Treating "absolute stability" merely as a concept of global stability can lead to the loss of important results for current applications. This review highlights numerous significant results, both old and contemporary, in the context of the study of absolute stability as per its origin in the Lurie problem.

This review reveals that despite being an old problem, the Lurie problem is still not completely solved. In other words, the search for necessary and sufficient conditions for absolute stability is ongoing, for example, as done by [8] for a class of 5th order Lurie-type systems. Current studies increasingly consider more general Lurie-type systems (e.g., [12, 26, 51]), i.e., with multiple nonlinearities, uncertainties, and delays. Many of these works find only sufficient conditions; however, in some cases, these conditions are less conservative than others, and many new results in this line have emerged. Therefore, finding the necessary and sufficient conditions is still a challenge in the context of the Lurie problem.

6.2. Review of the Lurie problem and its applications to the medical and biological fields

The review of the Lurie problem and its applications in the medical and biological fields was carried out using the PRISMA methodology (presented in Section 2), which provides a transparent and extensive article selection process. The result of the search using the PRISMA methodology is presented throughout Section 5, where interesting papers using Lurie systems and the theory of absolute stability have been presented. At the same time, discussions were held indicating possibilities for future research, some of which are highlighted in the following paragraphs. The review has shown the wide application of the Lurie problem in neuroscience, from its relationship with ANN to recent applications to Alzheimer's and Parkinson's disease. In particular, it was shown that HNN can be considered a stricter case of Lurie-type systems. In this vein, future research could further explore the applications of Lurie-type control systems, offering significant innovations for the treatment of pathologies in neuroscience. For instance, the refinements to the ALD models, as introduced by [3,43]. In addition, these studies suggest that future research should include *in silico* implementations and validations with real data, which could pave the way for *in vivo* experiments (when technology allows) and enable new therapeutic approaches.

It was noted in the review of medical and biological applications that older theories, such as the circle and Popov criterion, have been used in some cases to obtain stability conditions. In these cases, the suggestions for future research include the application of more recent theories, such as those presented in Section 4 or some presented throughout the work (for example, [12, 24, 26, 28, 49, 51]), which can provide less conservative and more accurate conditions. Specifically in areas such as anesthesiology, endocrinology, epidemiology, medical devices, and oncology, the application of more recent conditions, such as the Theorems 4–7, can significantly optimize results. Furthermore, extending the theorems can be done to deal with specific cases, enabling more precise and effective solutions in particular situations.

The review did not find many applications of the Lurie problem in cardiology, which is a very significant area in medicine. However, it is noted that some problems in this area, for example, [94–96], can be put into Lurie-type system form, and thus the theories derived from research into the Lurie problem can be applied to improve the performance of these cardiac devices. Finally, several other real-world systems can be intentionally transformed into Lurie-type systems in order to utilize the theory of absolute stability. This idea can be taken as a final suggestion for future research, namely, to search the literature for mathematical models which could be set up as Lurie-type systems.

Author contributions

R. F. Pinheiro: conceptualization, investigation, formal analysis, methodology, writing-original draft; R. Fonseca-Pinto: investigation, methodology, funding acquisition, supervision, project administration, writing – review and editing; D. Colón: conceptualization, formal analysis, investigation, supervision, writing-review and editing. All authors have read and agreed to the published version of the article.

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Conflict of interest

The authors declare that they have no conflicts of interest.

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