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Positive dynamical systems: New applications, old problems

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Abstract: This review paper presents four relevant and very recent real-world application problems demanding developments of long–standing theoretical open problems in the field of positive systems research. Notably, the selected applications belong to very different fields of science and technology, ranging from biology and medicine to civil and electronic engineering. This clearly shows how pervasive positive systems are in mainstream research. Additionally, the theoretical issues stemming from these applications are the living proofs of how the apparently *simple* positivity constraint on the variables of interest makes the theory behind practical problems far from trivial, even for the linear case.

Keywords: external positivity, minimal positive realization, positive system, structural positive controllability.

1. INTRODUCTION

A positive system is a dynamical system in which the state variables are always positive (or at least nonnegative) in value. A formal definition for a single-input/single-output linear time-invariant finite-dimensional dynamical system is the following:

$$\begin{aligned} \dot{x}(t) &= Ax(t)+bu(t) & x(k+1) &= Ax(k)+bu(k) \\ y(t) &= cx(t)+du(t) & y(k) &= cx(k)+du(k) \end{aligned}$$

for the continuous-time case and the discrete-time case. The vectors $x(t), x(k) \in \mathbb{R}^n$ collect the state variables, while $u(t), u(k) \in \mathbb{R}$ and $y(t), y(k) \in \mathbb{R}$ are the input and output variables, respectively. Such systems are said to be *positive* if the state and output variables are nonnegative for all times for each nonnegative initial condition $x(0)$ and each nonnegative input. Necessary and sufficient conditions require the matrix A to be a Metzler matrix (nonnegative matrix) for the continuous (discrete) case. Moreover, matrices b, c and d must be nonnegative matrices.

Surprisingly, it is quite easy to obtain the information on state variables positivity in the face of the huge impact that this property has on the system's dynamics. This feeling of surprise is well expressed by Professor Luenberger in his book on dynamic systems:

The theory of positive systems is deep and elegant – and yet pleasantly consistent with intuition. [...] It is for positive systems, therefore, that dynamic systems theory assumes one of its most potent forms. [...] Indeed, just the knowledge that the system is positive allows one to make some fairly strong statements about its behaviour: these statements being true no matter what value the parameters may happen to take. [1]

As a matter of fact, there are many real-world applications of positive systems theory in diverse areas of science and technology. The reason is that positivity is virtually always directly related to the nature of the phenomenon at hand. It suffices to observe that any sort of resource is measured by a positive quantity (money, goods, time, queues, buffers size, data packets, human, animal, and plant populations, the concentration of any substance such as mRNAs, proteins, molecules, electric charge, light intensity levels...). Obviously, also stochastic models, such as the Hidden Markov Model (HMM), are positive systems.

Basic results on the theory of positive systems can be found in [2]. Many advanced issues regarding positive system analysis and control have been studied by a large number of authors from the '70s. Just to cite a few: controllability [3–6], stabilization [7,8], behavioural approach [9,10], optimal control [11], identification [12], realization [5, 13–18] and switched systems [19].

In this review paper, four selected promising real-world applications of positive systems theory are discussed. These applications, although related to the seemingly simple case of linear, time–invariant positive dynamical systems, demand developments of long–standing theoretical open problems in the field of positive systems research.

Notably, the selected applications belong to very different fields of science and technology, ranging from biology and medicine to civil and electronic engineering. This clearly shows how pervasive positive systems are in main-

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stream research. Additionally, the theoretical issues stemming from these applications are the living proofs of how the apparently *simple* positivity constraint on the variables of interest makes the theory behind practical problems far from trivial, even for the linear case. This short review aims to provide a bird's-eye presentation of the applications and a sketch of the corresponding theoretical issues, referring the interested reader to the relevant literature on the topics reported in the bibliography.

The paper is organized as follows. Problems related to the analysis of complex biological networks are illustrated in Section 2. A key issue in these problems, and especially in the field of molecular biology, is the constraint due to the positivity of state variables that are the concentration of some molecular species, e.g., a protein, a transcript, or a metabolite. Precisely, it has been shown that the study of reachability properties of complex networks may open a new framework for the study of biological processes at the molecular scale. Section 3 illustrates two different problems related to the determination of minimal positive state-space description of positive systems. The first one concerns drug kinetics and the determination of internal structures of a compartmental model when its impulse response is measured through an input-output experiment (e.g., a bolus in the bloodstream). An immediate application in clinical medicine of this theoretical problem is the determination of the (minimum) number of organs involved by the drug response of the body. In this case, the state variables of the model represent drug concentrations and, as such, are bounded to be nonnegative over time. The second problem considered is the design of digital filters using two different technologies: optical fibers and charge-coupled devices. In these devices, the state variables of the filter are bounded to be nonnegative given that they represent intensity levels of light signals and sizes of the charge packets, respectively. The intelligent vehicle–highway system is briefly described in Section 4 to introduce the problem of collision avoidance between vehicles in a platoon without communication. This problem is nothing but the design of a vehicle controller achieving externally positive closed–loop dynamics and, interestingly, there is still no general design procedure for that purpose. Moreover, the question of when such a controller exists has not been clarified yet even thougt this problem has been raised half a century ago. Concluding remarks are given in Section 5.

2. POSITIVITY IN BIOLOGICAL NETWORKS

Complex networks science is the study of networks with a focus on *emergent properties*. The fundamental tenet is that relationships (links) among elements (nodes) are much more relevant than the nature and properties of the elements themselves. A prototypical example is the field of social sciences where the study of networks has a long history of theoretical developments and applications. Usually, nodes are individuals and links are relationships among them (such as friendship or the like): the emergent property of interest is the result of *collective behavior* produced by blind, and possibly independent, individual choices leading to an organized complexity, where macroscopic laws emerge from microscopic *chaos*. The underlying hypothesis just described resembles that of thermodynamics, where the emergent property of temperature does not belong to any single particle of matter but to the system as a whole. This powerful metaphor forms now the rational basis for many other fields of research besides social sciences. Recently, the development of technologies able to measure quantitatively at the molecular level the state of a cell and produce a huge quantity of data, has revitalized this metaphor and, as a consequence, network properties of interest for the social sciences has been directly exported to the relatively new science of molecular biology. The so-called *omics* data are produced at an ever-increasing rate. Starting with the sequencing of the human genome in the year 2003, the biological and medical community has witnessed an impressive quantity of new information and discoveries about life and disease. More importantly, this rapid growth of biological quantitative data has gone hand in hand with the awareness that life and disease are not related to an organized top-down control structure, but rather to an intricate network of many interacting players. The study of emergent properties of biological networks has therefore become the new frontier for research in the study of life and disease. For example, the concept of a *silver bullet* targeting a single specific protein (typically a receptor protein) responsible for a disease, is definitely behind us, as shown in Figure 1.

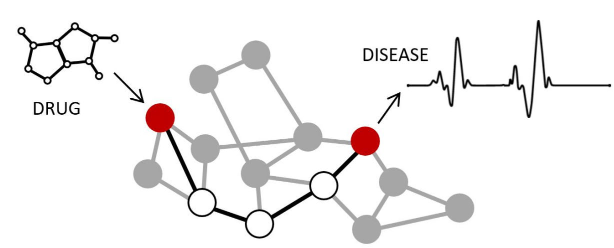

Fig. 1. Targeting proteins in the omics era. The *perfect drug* paradigm to cure a disease by targeting a single protein has been replaced by the concept of perturbing a module of disease proteins through a path on the protein-protein interaction network from a target to a disease protein.

2.1. New application: Network medicine

We are now living in the era of *network medicine* [20], that is the era in which disease is not simply considered as the malfunctioning of a single gene (or tissue or organ) in isolation, but it is considered as the result of a myriad of small changes or perturbations in a dense network of relationships among a wide variety of molecular players, including proteins, messenger RNAs [21], non-coding RNAs, transcription factors, epigenetic modifications of chromatin, bacteria in the gut, and many others. The huge amounts of biomedical *big data* and its integration by means of computational tools provided by the so-called *data science*, provide the opportunity to push the boundaries of medicine far beyond the current situation. Bioinformatic technologies have paved the way for the creation of large databases of previously unheard dimensions in clinical research. We are close to a scenario where the available data are of unprecedented amount and quality: the challenge is to make biological sense of such data.

2.2. Old problem: Reachability

A recent promising development in network medicine is the study of complex networks embedded in a dynamical system. Nodes are then state variables and the underlying network defines the structure of a multivariable dynamical system. For example, in a cell, the state variables may represent the amount of gene products (proteins and RNAs) and, therefore, the fate of a cell (e.g., tissue type) corresponds to a specific region of the state space. It is therefore of paramount importance to study if and how the inputs (e.g., cellular micro-environmental factors) determine the cell's state. From a mathematical point of view, this corresponds to the reachability problem for a dynamical system, i.e. that of determining whether a desired final state can be *reached* starting from a given initial state using an appropriate input function. This mathematical problem can be solved in general by considering the so-called *reachable set*, that is the set of all states reachable from the initial state. A fundamental problem is to determine conditions for the reachable set to be the entire state space for a given network topology. Such conditions have been presented by Liu and coworkers [22] by identifying a minimal set of independent inputs (*driver* nodes) for arbitrary network topologies and sizes able to fully control the dynamics. The underlying idea is to consider only the non-zero entries of the dynamic matrix (i.e., the links of the network) and then look for the nodes to be used as inputs (drivers) able to ensure reachability of the entire state space. This approach has been successfully applied to the gene regulatory network of type-2 diabetes to reveal a novel transcription factor that regulates key disease-related genes [23], to a directed human interaction network for the determination of novel putative disease genes and drug targets [24] and to multiple biological networks to highlight new potential therapeutic targets in osteosarcoma [25]. The authors developed a maximum multiplicity theory to define network controllability by means of the minimum number of controllers and independent driver nodes. Furthermore, Li et al. [26] used a general framework to prove that temporal networks can reach controllability faster, with less control energy, and more compact control trajectories, compared to their static counterparts. Results on the dual property of observability of complex networks are presented in [27].

As discussed above, the main application of reachability analysis is in the field of biological dynamic networks, and it is particularly useful for the very large networks obtained from multi-omics data, such as the protein interaction network, the metabolic network, or the gene regulatory network. It goes without saying, that a key issue in complex biological networks analysis is the positivity constraint on state variables, which are always positive being the amount or concentration of some molecular species (e.g., protein, transcript, or metabolite). It is worth noting that the results just described do not take into consideration the positivity of the variables and therefore more appropriate approaches can be envisaged since many results are already available for positive systems. In particular, necessary and sufficient conditions for the reachable set of discrete-time positive systems to be the entire positive orthant are presented in [3]: the positive orthant is reachable (in a finite or infinite number of steps) if and only if the matrix defined by the aggregation of vectors $A^k b$ for $k = 1, 2, \cdots$, contains a monomial submatrix. A network-theoretic version of the same result has been presented in [28]. The authors proved that the reachable set of a positive discrete-time linear system is the positive orthant iff the associated network contains a deterministic path starting from a vertex and reaching any other vertex [29]. When the reachable set is not the entire positive orthant, in general, it is a cone therein contained. The shape of such a cone, in the discrete-time case, has been studied in [30]. It is there shown that this set may be very difficult to compute in practice since, even if polyhedral, the cone may have an infinite number of edges.

3. POSITIVITY IN MODEL STRUCTURES

3.1. New application: Compartmental model structures identification

Pharmacokinetics is defined as the study of the time course of drug and metabolite levels in an organism and of the mathematical techniques required to develop formal models able to provide biological insight to data. Compartmental modeling of drug kinetics is commonly used to elucidate drug concentration changes in the bloodstream over time by considering a finite number of interconnected subsystems, called compartments, interacting one each other by exchanging material (e.g., drugs), as shown in Figure 2. A single compartment generally corresponds to an organ or tissue type in which drug distribution is assumed perfectly well mixed and uniform. For example, drug concentration into adipose tissue may well

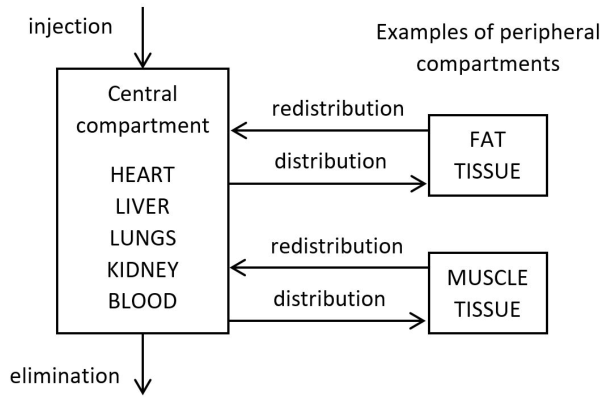

Fig. 2. Compartmental model. The dynamics of a drug in the body tissues can be very complex, as several processes such as absorption, distribution, and elimination, work to alter drug concentrations. Compartmental models are then used to predict a drug's behavior in the body and determine the amount of the dose to be administered.

differ from that of renal tissue in most cases and, consequently, these tissues are usually separated and modeled by different compartments. Highly perfused organs (like the heart, liver, and kidneys) often have similar drug concentration patterns, so these areas may be considered as one compartment. Obviously, there are no general rule for determining the *right* number of compartments and the ultimate choice is more an art than a science. The state variables of the model represent the concentration of the drug in each compartment and, as such, are bounded to be positive (nonnegative) over time. In this context, one of the most important open problems is the determination of internal structures - specifically the number of compartments – when the impulse response (e.g., the plasmatic level of a drug) is measured through an input-output experiment [31], which usually consists of the injection of a drug bolus into the bloodstream. In other words, only the compartmental nature of the model is assumed, whilst the number of compartments may not be known *a priori* and should be therefore determined from the measured data. An immediate application of this problem in clinical medicine is the identification of the number of organs involved by the drug response of the body. In terms of positive systems theory, the problem is then that of determining a positive state-space description of minimal dimension that explains the measured data.

3.2. New application: Digital filter design

Digital signal processing consists of the representation of signals using sequences of numbers for data processing tasks. Such tasks can be, for instance, compression and transmission of signals, filtering for smoothing, or noise reduction. In the linear case, filters may be represented by their transfer functions that represent, in an appropriate domain, the relation between the input and output sequences. The physical implementation of a filter calls for specific devices for delays, products, and sums. These devices may be of very different nature, depending on the considered technology. If the latter forces the utilization of devices requiring only positive values for products, the filter design is nothing but a positive state-space realization of the filter transfer function. Minimality of such a realization allows then to reduce space occupation and power consumption of the filter. This situation occurs in the case of two technologies such as optical fibers and charge-coupled devices.

Optical fibers are characterized by low-loss (fractional decibels/kilometer) and large bandwidth-length product (on the order of 100GHz km for single-mode fibers). In particular, optical filters are often used for high-speed signals processing in a waveguide format. This allows avoiding costly electro-optic and optoelectronic conversions and possible electronic bottlenecks. As shown in [32], if the coherence time is small enough, the input signal of an optical filter may be modulated as light intensity amplitude. In this case, the state variables of the filter represent the intensity levels of light signals and consequently are bounded to be positive (nonnegative) over time.

Charge routing networks (CRNs) were developed at the Bell Labs [33] to achieve discrete-time signal processing on a MOS integrated circuit chip. The advantage of this technology is lighter weight, smaller size, lower power consumption, and improved reliability (with respect to an equivalent standard implementation). CRNs move quantities of electrical charge in a controlled way across a semiconductor substrate under the application of a sequence of clock pulses. Precisely, these devices consist of a set of storage cells, locations where a packet of charge can be stored and maintained isolated from the others, and of a specific periodically repeating routing procedure that splits and transfers these charge packets among the cells. The state variables of the filter represent then the size of the charge packets in the cells and are bounded to be positive (nonnegative) over time.

3.3. Old problem: Minimal realizations

The problem of determining a positive state-space description of a given transfer function or impulse response is inherently different and challenging from that of ordinary systems [14]. In fact, the matrices of the realization must have a specific sign pattern and, consequently, a positive realization may not exist at all. Precisely, when considering generic linear systems, a minimal state-space realization is always both controllable and observable and its dimension corresponds to the rank of the Hankel matrix and the order of the system transfer function. This fact may not hold true for positive realizations. In fact, a minimal positive realization is - in general - not controllable nor observable so that its dimension may be larger than the order of the transfer function of the system [34]. Interestingly, the nonnegative rank of the Hankel matrix is only a lower bound for the dimension of a minimal positive realization [35]. Although necessary and sufficient conditions for the existence of a positive state-space realization of a positive system have been given in [13, 15], minimality whilst retaining positivity is still an unsolved theoretical problem. Conditions for a positive realization to be minimal have been given only for special classes of positive systems such as the tree compartmental systems considered in [31] and the positive reachable systems in [36]. Further results are given in [37–39]. The case of third-order transfer functions with real poles having a third-order (minimal) positive realization is considered in [40, 41]. To date, only lower and upper bounds for the dimension of a minimal positive realization have been given, see [37, 42–45]. In more detail, an upper bound for transfer functions with only real and simple poles and a lower bound for generic transfer functions are provided in [44]. The result on the upper bound is then improved in [37] and extended to the case of simple complex poles in [43]. Moreover, a refinement of the lower bound is provided in [42] exploiting some properties of the dominant eigenvalues of nonnegative matrices. In [45], a lower bound is given for a very special class of transfer functions, i.e., those for which there exists a time instant at which the nonnegative impulse response value is zero and is strictly positive from that instant onwards.

4. POSITIVITY IN MULTI-AGENT MODELS

Highway traffic congestion has increased dramatically in the last decades in any part of the world, independently of its development level, and there is no clue that it will stop to get worse. The reason is that the existing roadways cannot bear the increasing number of automobiles. The apparent effect is a progressive reduction in traffic fluidity, resulting in larger journey times, fuel consumption, and environmental pollution, as compared with an uninterrupted traffic flow. Moreover, the last 50 years have proved that the broadening of the highway network to cope with congestion does not solve traffic problems in the long term. The only possibility to effectively tackle congestion is to manage traffic. This can be accomplished using a wide variety of techniques, including avoiding bottlenecks, prioritizing multi-occupancy vehicles, and discouraging users to use the car at rush hours. However, the best opportunity in the years to come may arise from the evolution of automotive technology towards fully automated vehicles embedded onto roadways. The key tenet is that of managing traffic in tightly spaced platoons, that is groups of automated vehicles following each other at a small distance and constant and uniform high velocity, as shown in Figure 3. Such traffic management alone could dramatically increase highways capacity [46] and, at the same time, reduce fuel need, and pollution, due to exploitation of slipstream.

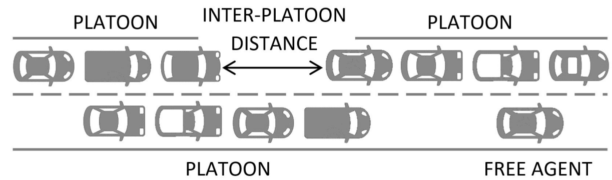

Fig. 3. The platooning concept. The inter-platoon distance is such that the lead vehicle in the rear platoon has enough time to slow down and avoid an accident. Hence, safety can be examined by evaluating only the possibility of collisions within a platoon.

4.1. New application: Collision avoidance

A big issue to be urgently addressed is obviously platoon safety. Precisely, it is needed to ensure collision avoidance within the platoon and this can be achieved only with automated vehicles since a human driver is not able to react in real-time to disturbances, due to the high platoon velocity and the small distance between vehicles. In general, collision avoidance can be obtained using two different control architectures: centralized or distributed. The first one requires a control unit for each vehicle, a centralized coordinating unit for each platoon, and a communication system between all the vehicles of the platoon. The second one is much easier to implement since it requires locally measurable quantities and a control unit for each vehicle. Such control must adapt the speed and keep a safe distance to the vehicle in front by simply monitoring the distance and its speed. The fundamental question is about which properties the controlled vehicles should have to avoid collisions in the platoon [47]. This question has been tackled by using the notion of *string stability* [48], which is a requirement on the platoon that avoids the disturbances amplifications along the vehicle string. A sufficient condition on string stability [49] requires a bounded error transfer function and was experimentally evaluated with a few vehicles [50]. However, it has been shown [47] that string stability is not an appropriate control aim when designing the local controllers for the vehicles. In fact, string stability is only a necessary, but not a sufficient condition for collision avoidance and any decentralized controller cannot achieve string stability [51]. Lunze [47, 52] proved that the controlled vehicles have to be externally positive systems with respect to their input (the speed of the preceding vehicle) and their outputs (vehicle speed and distance from the preceding vehicle). This condition on the dynamics of the controlled vehicles is the necessary and sufficient condition for simultaneously guaranteeing time-headway spacing and collision avoidance in platoons. Vehicles with these properties can then be combined into platoons of arbitrary length.

4.2. Old problem: External positivity conditions

A linear system is said to be externally positive if its output is nonnegative for any nonnegative input [2]. This is the case if and only if the impulse response of the system is always nonnegative or, equivalently, the step-response has no overshoot, and in general, it stems directly from the specific problem at hand. Properties of such systems (not necessarily positive) are reviewed in [53]. It is plain that, for example, a positive system - that is a system in which all the inputs, outputs, and state variables are always nonnegative - is certainly an externally positive system. However, a systematic procedure to check external positivity, given the transfer function, is not available so far. A robust regulator for systems with nonnegative impulse response is proposed in [54], thus recognizing the relevance of the problem for process industries when flows, levels, concentrations, and temperatures are the variables of interest. However, conditions on the pole-zero pattern are not provided. Interestingly, a few years earlier, a sufficient condition for an in-line pole-zero pattern (i.e., alternate complex conjugate pole-zero positions along the same real line) was presented in [55]. The problem of designing controllers for discrete-time linear plants that render the closed-loop impulse response nonnegative is studied in [56]. It is there proved that the necessary and sufficient condition on the plant for the existence of a compensator that makes the closed-loop impulse response sign invariant is that there be no real, positive, nonminimum phase plant zeros. In [57, 58] sufficient conditions to avoid overshoot in the step response of a linear system with stable real zeros and poles are given. This condition is directly related to the pole-zero configuration of the corresponding transfer function and is based on the result presented in [59] which provides an upper bound for the number of extrema of the step-response based on the location of the zeros of a system. Recently, conditions for external positivity were given in [60]. These conditions are in the time domain and use the properties of the weak majorization of vectors. Finally, a characterization of external positivity, based on the Post formula for Laplace inversion, is given in [61]. In general, however, the design of control laws that achieve externally positive closed-loop dynamics is still an open problem [62].

5. CONCLUSIONS

In this paper, four very recent application problems in the field of positive systems research have been presented and the corresponding theoretical issues discussed. In closing, note that extensive research activities have been devoted to classes of systems that are extensions of the class of positive systems here considered. In particular, several properties of 2D linear positive systems [63–65] and positive linear systems with delays [66, 67] have been investigated. Finally, even if an extension to the nonlinear case is far from trivial, several results are available for specific classes of nonlinear systems such as the cooperative and monotone systems [68–70]. Space constraints does not allow a detail discussion on these topics. All these arguments witness how this field of research is still alive and kicking.

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