2016 American Control Conference (ACC)
Boston Marriott Copley Place
July 6-8, 2016. Boston, MA, USA

# Structural Analysis and Design of Dynamic-Flow Networks: Implications in the Brain Dynamics

Sérgio Pequito [†] Ankit N. Khambhati [♮,♭] George J. Pappas [†] Dragoslav D. Šiljak [‡]
Danielle Bassett [†,♮,♭] Brian Litt [♮,♭,♯]

***Abstract*— In this paper, we study dynamic-flow networks, i.e., networks described by a graph whose weights evolve according to linear differential equations. Further, these linear differential equations depend on the incidence relation of the edges in a node, and possibly nodal dynamics. Because some of these weights and their dependencies may not be accurately known, we extend the notion of structural controllability for dynamic-flow networks, and provide necessary and sufficient conditions for this to hold. Next, we show that the analysis of structural controllability in dynamic-flow networks can be reduced to that of a digraph which we refer to as *meta* digraph. In addition, we consider different actuation capabilities, i.e., we assume that both the nodes and edges in the dynamic-flow network can be actuated, and we explore the implications in terms of computational complexity when the minimum cost-placement of actuators is considered.**

**The proposed framework can be used to identify actuation capabilities required to mitigate epileptic-brain dynamics. More precisely, the functional connectivity of mesoscale brain dynamics can be modeled as a dynamic-flow network by considering dynamic functional connectivity of the network. In the context of epilepsy, the modeling is motivated by new findings that show that the edges within seizure-generating areas are almost constant over time, whereas the edges outside these areas exhibit higher variability over time in human epileptic networks. In addition, implementable devices to control drug-resistant seizures by affecting the epileptic network has gained considerable attention as a viable treatment option. Subsequently, from a control-theoretic perspective, one can consider actuation to attenuate edge variability responsible for seizure-generation in the epileptic network. In particular, we address the following two scenarios: (i) current placement of electrical stimulators, and their probable capabilities; and (ii) determine the minimum cost placement with minimum actuation capabilities. The latter problem is motivated by the fact that some edges may correspond to more accessible (or less harmful) regions in the brain, whereas others might correspond to sensitive regions in the brain.**

## I. INTRODUCTION

Complex networks have traditionally been studied by resorting to graphs [1]. These have been considered most of the times as static objects, whose weights associated with the edges are assumed constant over time. However, this is a rather rigid description that often fails to adequately represent the structure of natural, social and man-made processes, especially in uncertain environments where the relations between the constituent parts change over time [2].

Dynamic-flow networks model dynamical systems captured by networks where the weights on the edges evolve according to linear differential equations. In addition, these linear differential equations depend on the incidence relation of the edges in a node, and possibly nodal dynamics. For example, in social networks, a node (representing an individual) constantly processes information received from its upstream neighbors and makes decisions that are communicated to its downstream neighbors. The information received and passed by a node can be represented by the state variables on its incoming and outgoing edges. Thus, mapping the signals of the incoming edges onto those of the outgoing edges. This is also the case in a network of computers and routers on the Internet, where the edges represent physical connections and the state variables on the edges represent the amount of packet flow along a particular connection in a given direction. The mechanism of the nodes then corresponds to a load-balancing or routing mechanism that allows packets to reach their destination while avoiding congestion.

Dynamic-flow networks can also be used to model functional brain networks, where nodes represent neural populations and edges are statistical relationships between neural activation patterns. In particular, these networks are suitable to capture the brain dynamics when *dynamic functional connectivity* is considered [3]. More specifically, a sliding-window over the blood-oxygen level dependent (BOLD) signal is considered to obtain over time the *functional connectivity* that captures the Pearson's correlation between signals. In particular, the local dependency on adjacent edges is justified by the spatial-temporal dependency of the BOLD signals [3].

The control of dynamic-flow networks was introduced in [4], and in this paper we aim to account for the case where the parameters describing the possible interaction dependencies in the flow-dynamic networks are either free or constant parameters over time. Towards this goal we resort to structural systems theory [5] that enables the introduction of generic controllability notions [6], i.e., controllability holds for almost all possible parameterization of the free parameters. Therefore, we aim to assess when flow-dynamic networks (seen as a dynamical system) are generically controllable. In addition, we assume that different functions and

This work was supported in part by the TerraSwarm Research Center, one of six centers supported by the STARnet phase of the Focus Center Research Program (FCRP) a Semiconductor Research Corporation program sponsored by MARCO and DARPA, and the NSF ECCS-1306128 grant.

[‡]Department of Electrical Engineering, Santa Clara University, Santa Clara, CA 95 053, USA

[†]Department of Electrical and Systems Engineering, School of Engineering and Applied Science, University of Pennsylvania

[♮] Department of Bioengineering, University of Pennsylvania

[♭] Penn Center for Neuroengineering and Therapeutics, University of Pennsylvania

[♯] Department of Neurology, Hospital of the University of Pennsylvania

978-1-4673-8681-4/$31.00 ©2016 AACC

locations of control inputs are possible, which influences the edges' weights and nodes' dynamics. More precisely, these can be *multi-node input*, i.e., the input signal is injected in several nodes to regulate how the dynamics of the outgoing edges changes, and *multi-edge inputs*, i.e., an input can actuate a linear combination of edges, not necessarily the ones that share vertices. Particular cases of these two are the *out-node inputs*, i.e., all the outgoing edges from a single vertex are driven by a scalar input signal, and the *in-edge inputs*, i.e., an input can actuate only a single edge dynamics directly. In this paper, we analyze and provide necessary and sufficient conditions for dynamic-flow networks, where parameters can be either free or constant over time, to be generically controllable. In addition, we consider the control placement problems under different assumptions; more precisely, we consider that different edges and/or nodes may incur in different costs.

*Related Work*

Several necessary and sufficient conditions that characterize the structural controllability, as well as their verification, are known for linear time-invariant [5], or switching systems [7]. Nevertheless, the selection, commonly referred to as design, of minimum actuation capabilities to ensure that these conditions hold has only been addressed in the last years. In the context of linear time-invariant systems, the problem of determining the minimum number of actuated variables ensuring structural controllability was addressed in [8], [9]. Later, it was extended to the case where the minimum cost is sought when the actuated state variables incur in a cost that does not depend on the actuator considered [10], and to the minimum cost problem allowing the actuation cost of a state variable to depend on the actuator considerez [11]. An alternative formulation consists in assuming a predefined collection of actuators from which one selects those to be used to ensure structural controllability, but in such scenario the problem of determining the minimum collection of such actuators is NP-hard [12]. Notwithstanding, some subclasses have been determined where the problem is polynomial, even when different actuation costs are considered [13]. More recently, actuation selection problems ensuring structural controllability were also proposed for discrete-time fractional dynamics [14], and switching systems for some switching policy [15] and for all switching policies [16].

In [17] is presented a framework that is close to ours, where *switch-board dynamics* is studied for the edges' dynamics and assumed to be controlled by *in-node inputs*, i.e., an external input is injected in the node from which the edges to be actuated depart. In addition, all the edges are actuated in equal manner, and the dynamics of a node is considered to be constant in time, which we refer to as *static node*. The analysis results in studying the *line/dual* graph, on which some actuation deployment strategies are provided. In this paper, we extend [17] in multiple ways: (i) we assume that the nodes can have dynamics; (ii) we deal with multi-node and multi-edge inputs; and (iii) some edges' weights may be constant over time. Furthermore, we notice that the analysis can no longer be done resorting to dual graphs, see Remark 1 for additional details. ∘

The main contributions of this paper are as follows: (i) we formally introduce the notion of generic controllability for dynamic-flow networks, where some edges' weights can be constant over time; (ii) we introduce necessary and sufficient conditions that ensure structural controllability; (iii) we address the problem of minimum actuator placement incurring in the minimum cost while ensuring structural controllability; (iv) we show how dynamic-flow networks can identify brain regions that should be actuated to ensure that edges' weights variations are kept within certain bounds; (v) we show that current actuation capabilities are enough to ensure structural controllability; and (vi) using real data, we determine the location of actuators to regulate the dynamics such that epileptic seizures may be attenuated and/or overcome.

The rest of the paper is organized as follows. In Section II, we provide the formal problem statement. Section III reviews some concepts from computational complexity and graph theoretical concepts used in structural systems theory. Section IV presents the main technical results, followed by a case study in Section V showing the implications in the brain dynamics; more specifically, in the context of epilepsy. Conclusions and discussions on further research are presented in Section VI.

## II. Problem Statement

Let $\mathcal{D}=(\mathcal{V},\mathcal{E})$ be a digraph, where $\mathcal{V}$ denotes a set of $n$ vertices, and $\mathcal{E}$ the set of $m$ directed edges been the vertices. In addition, consider that each edge in the digraph has *weight* $w$ associated with it, where $w:\mathcal{E}\to\mathbb{R}_0^+$, and a label $\mu(e)\in\{1,\star\}$, for $e\in\mathcal{E}$, where $\mu(e)=1$ indicates that the weight is constant over time and $\mu(e)=\star$ indicates that it varies over time. Further, let $\mathbb{N}=\{N_i\}_{i\in\mathcal{I}}$ represent the multi-node actuation signal, where the collection of the nodes' set $N_i\subset\{1,\ldots,n\}$ is actuated by the actuator $i$. In particular, if every $N_i$ contains only one node than we have out-node inputs. Similarly, let $\mathbb{E}=\{E_j\}_{j\in\mathcal{J}}$ be the collection of the edges' set $E_j\subset\mathcal{E}$ actuated by the actuator $j$, and if every $E_j$ contains only one edge than we have in-edge inputs. Consequently, the dynamic-flow network can be described by $(\mathcal{D}=(\mathcal{V},\mathcal{E}),w,\mu,\mathbb{E},\mathbb{N})$, where it is implicitly assumed that the dynamics of one edge depends on a linear combination on the incoming edges' weights. A dynamic-flow network is *structurally controllable*, if there exits control signals delivered to the dynamic-flow network by $(\mathbb{E},\mathbb{N})$ such that the edges' weights can be steered to an arbitrary value, for almost all free parameters describing edge dynamics.

Therefore, we are interested in addressing the following problems:

- $\mathcal{P}_1$ When is the dynamic-flow network $(\mathcal{D},w,\mu,\mathbb{E}=\{E_j\}_{j\in\mathcal{J}},\mathbb{N}=\{N_i\}_{i\in\mathcal{I}})$ structurally controllable?
- $\mathcal{P}_2$ Consider a structurally controllable dynamic-flow network $(\mathcal{D}=(\mathcal{V},\mathcal{E}_{\mathcal{V},\mathcal{V}}),w,\mu,\mathbb{E}=\{E_j\}_{j\in\mathcal{J}},\mathbb{N}=\{N_i\}_{i\in\mathcal{I}},\{c_j^E\}_{j\in\mathcal{J}},\{c_i^N\}_{i\in\mathcal{I}})$, where $c_j^E$ and $c_i^N$ are the actuation costs associated with $E_j$ and $N_i$, respec-

tively. What is the minimum $|\mathcal{I}|$ and $|\mathcal{J}|$ that ensures the lowest cost and structural controllability?

## III. PRELIMINARIES AND TERMINOLOGY

We start by reviewing some computational complexity concepts [18], followed by some graph theoretic concepts related with the study of structural systems theory [5], [9].

A (computational) problem is said to be *reducible in polynomial time* to another if there exists a procedure to transform the former to the latter using a number of operations which is polynomial in the size of its elements. Such a reduction is useful in determining the complexity class that a problem belongs to [18]. For instance, a problem $\mathcal{P}$ in NP (i.e., the class of non-deterministic polynomial algorithms) is said to be NP-complete if all other NP problems can be polynomially reduced to $\mathcal{P}$ [18]. The NP-complete class is used to describe the complexity of decision versions of problems. For instance, the following constitutes a decision problem that is particularly relevant in the design of structural systems context [12]: Given the structural dynamics' matrix and a collection of possible inputs, is there a collection of inputs with exactly $k$ elements, such that the system actuated by these is structurally controllable?

Alternatively, it is often natural to consider the optimization versions associated with the decision problems. For instance, the optimization version of the problem stated above aims to determine the minimum $k$ such that the aforementioned property holds. This optimization problem is referred to as the *constrained minimum structural input selection* (CMSIS) problem [12]. Note that, if a solution to the optimization problem is known, the decision problem is straightforward to solve. Consequently, the optimization problem formulations of NP-complete problems, are referred to as being NP-hard, since they are at least as difficult as the NP-complete problems; in other words, by solving an instance of the optimization problem (the NP-hard problem), one can obtain a solution to an NP-complete problem. Finally, we notice that CMSIS is a NP-hard problem [12].

Consider a linear time-invariant system described by

$$\dot{x} = Ax + Bu, \tag{1}$$

where $x \in \mathbb{R}^n$ denotes the state and $u \in \mathbb{R}^p$ the input. In addition, $A$ is the $n \times n$ matrix describing the autonomous dynamics and $B$ the $n \times p$ input matrix describing the actuated state variables from each input. Suppose that the sparsity pattern, i.e., location of zeros and (possibly) nonzeros, of $A$ and $B$ is available, but the specific numerical values of the remaining elements is not known. Subsequently, let $\bar{A} \in \{0,1\}^{n\times n}$ (respectively $\bar{B} \in \{0,1\}^{n\times p}$) is the binary matrix that represents the structural pattern of $A$ (respectively $B$), i.e., it encodes the sparsity pattern of $A$ (respectively $B$) by assigning 0 to each zero entry of $A$ (respectively $B$) and 1 otherwise.

The following standard terminology and notions from graph theory can be found, for instance, in [9]. Let $\mathcal{D}(\bar{A}) = (\mathcal{X}, \mathcal{E}_{\mathcal{X},\mathcal{X}})$ be the digraph representation of $\bar{A}$ in (1), where the vertex set $\mathcal{X}$ represents the set of state variables (also referred to as state vertices) and $\mathcal{E}_{\mathcal{X},\mathcal{X}} = \{(x_i, x_j) : \ A_{ji} \neq 0\}$ denotes the set of state edges. Similarly, we define the following digraphs: $\mathcal{D}(\bar{A}, \bar{B}) = (\mathcal{X} \cup \mathcal{U}, \mathcal{E}_{\mathcal{X},\mathcal{X}} \cup \mathcal{E}_{\mathcal{U},\mathcal{X}})$ where $\mathcal{U}$ represents the set of input vertices and $\mathcal{E}_{\mathcal{U},\mathcal{X}} = \{(u_i, x_j) : \bar{B}_{ji} \neq 0\}$ the set of input edges.

A digraph $\mathcal{D}_s = (\mathcal{V}_s, \mathcal{E}_s)$ with $\mathcal{V}_s \subset \mathcal{V}$ and $\mathcal{E}_s \subset \mathcal{E}$ is called a *subgraph* of $\mathcal{D}$. If $\mathcal{V}_s = \mathcal{V}$, $\mathcal{D}_s$ is said to *span* $\mathcal{D}$. A sequence of directed edges $\{(v_1, v_2), (v_2, v_3), \cdots, (v_{k-1}, v_k)\}$, in which all the vertices are distinct, is called *an elementary path* from $v_1$ to $v_k$, as well as a vertex in a digraph with no incoming and outgoing edges (with some abuse of terminology). A vertex with an edge to itself (i.e., a *self-loop*), or an elementary path from $v_1$ to $v_k$ comprising an additional edge $(v_k, v_1)$, is called a *cycle*. Finally, a subgraph with some property $P$ is *maximal* if there is no other subgraph $\mathcal{D}_{s'} = (\mathcal{V}_{s'}, \mathcal{E}_{s'})$ of $\mathcal{D}$, such that $\mathcal{D}_s$ is a subgraph of $\mathcal{D}_{s'}$, and $\mathcal{D}_{s'}$ satisfies property $P$. Subsequently, a digraph $\mathcal{D}$ is said to be strongly connected if there exists an elementary path between any pair of vertices. A *strongly connected component* (SCC) is a maximal subgraph $\mathcal{D}_S = (\mathcal{V}_S, \mathcal{E}_S)$ of $\mathcal{D}$ such that for every $v, w \in \mathcal{V}_S$ there exists a path from $v$ to $w$ and from $w$ to $v$.

## IV. MAIN RESULTS

In this section, we present the main results of the present paper. First, we show that the dynamic-flow network can be written in terms of a state-space representation, which we refer to as *meta* digraph. In particular, a systematic procedure to construct this digraph is presented in Algorithm 1. Then, using the meta digraph, we obtain necessary and sufficient conditions to ensure structural controllability of the dynamic-flow network (Theorem 1); hence, providing an answer to $\mathcal{P}_1$. Subsequently, due to the proposed reduction from the dynamic-flow network to the meta digraph, and the fact that a meta digraph can be an arbitrary digraph (Theorem 3), we can obtain a series of results that dictate the computational complexity of the problem presented in $\mathcal{P}_2$ as well as its variations; more precisely, the general problem is NP-hard, but a polynomial complexity procedure can be used to determine solutions to a subclass of $\mathcal{P}_2$.

The polynomial reduction from a dynamic-flow network to the meta digraph is presented in Algorithm 1. This reduction allow us to provide a characterization of the solutions to $\mathcal{P}_1$, as described in the next theorem.

*Theorem 1:* The dynamic-flow network $(\mathcal{D} = (\mathcal{V}, \mathcal{E}_{\mathcal{V},\mathcal{V}}), w, \mu, \mathbb{E} = \{E_j\}_{j\in\mathcal{J}}, \mathbb{N} = \{N_i\}_{i\in\mathcal{I}}, \{c_j^E\}_{j\in\mathcal{J}}, \{c_i^N\}_{i\in\mathcal{I}})$, where $c_j^E$ and $c_i^N$ are the actuation costs associated with $E_j$ and $N_i$ respectively, is structurally controllable if and only if the meta digraph described by the pair $(\bar{E}, \bar{B})$ obtained from Algorithm 1 is structurally controllable. In addition, the actuation cost achieved by the deployed actuation capabilities in either digraph is the same. $\diamond$

*Proof:* The proof follows by structural induction; more precisely, we show that there are few atomic structures that hold and the result follows by noticing that any graph consists in a combination of these atoms. First, consider the case where one node has several incoming and outgoing

**ALGORITHM 1:** Determine the meta digraph from the state digraph.

**Input:** The dynamic-flow network and actuation costs $(\mathcal{D} = (\mathcal{V}, \mathcal{E}_{\mathcal{V},\mathcal{V}}), w, \mu, \mathbb{E} = \{E_j\}_{j \in \mathcal{J}}, \mathbb{N} = \{N_i\}_{i \in \mathcal{I}}, \{c_j^E\}_{j \in \mathcal{J}}, \{c_i^N\}_{i \in \mathcal{I}})$.

**Output:** Meta digraph $\mathcal{D}^*(\bar{E}, \bar{B}) = (\mathcal{E}^* \cup \mathcal{U}^*, \mathcal{E}_{\mathcal{E}^*,\mathcal{E}^*} \cup \mathcal{E}_{\mathcal{U}^*,\mathcal{E}^*})$ and actuation cost $c_k$ associated with the input $u_k$, for $k = 1, \ldots, |\mathcal{I}| + |\mathcal{J}|$.

$\mathcal{E}^* = \emptyset$; $\mathcal{U}^*(\mathbb{E}) = \emptyset$; $\mathcal{U}^*(\mathbb{N}) = \emptyset$; $\mathcal{U}^* = \emptyset$;
$\mathcal{E}_{\mathcal{E}^*,\mathcal{E}^*} = \emptyset$; $\mathcal{E}_{\mathcal{U}^*,\mathcal{E}^*} = \emptyset$; $\mathcal{E}_{\mathcal{U}^*(\mathbb{E}),\mathcal{E}^*} = \emptyset$; $\mathcal{E}_{\mathcal{U}^*(\mathbb{N}),\mathcal{E}^*} = \emptyset$;

1: $\mathcal{E}^* = \{e \in \mathcal{E}_{\mathcal{V},\mathcal{V}} : \mu(e) = \star\}$;
2: $\mathcal{U}^*(\mathbb{E}) = \{u_j : j \in \mathcal{J}\}$ where the cost of input $u_j$ is $c_j^E$ for $j \in \mathcal{J}$.
3: $\mathcal{U}^*(\mathbb{N}) = \{u_{|\mathcal{J}|+i} : i \in \mathcal{I}\}$ where the cost of input $u_{|\mathcal{J}|+i}$ is $c_i^N$ for $i \in \mathcal{I}$.
4: $\mathcal{U}^* = \mathcal{U}^*(\mathbb{E}) \cup \mathcal{U}^*(\mathbb{N})$;
5: $\mathcal{E}_{\mathcal{E}^*,\mathcal{E}^*} = \{(e, e') \in \mathcal{E}^* \times \mathcal{E}^* : e \rightsquigarrow e'\}$, where $e \rightsquigarrow e'$ denotes a directed path with the first and last edges being $e$ and $e'$ respectively, $\mu(e) = \mu(e') = \star$ and any other edge $e''$ in-between (if any) has constant weight over time, i.e., $\mu(e'') = 1$;
6: $\mathcal{E}_{\mathcal{U}^*(\mathbb{E}),\mathcal{E}^*} = \{(u_j, e) : e \in E_j\}$;
7: $\mathcal{E}_{\mathcal{U}^*(\mathbb{N}),\mathcal{E}^*} = \{(u_{|\mathcal{J}|+i}, e \equiv (k,l)) : e \in \mathcal{E}, k \in N_i, \mu(e) = \star\} \cup \{(u_{|\mathcal{J}|+i}, e') : e \equiv (k,l) \in \mathcal{E}, k \in N_i, \mu(e) = 1, e \rightsquigarrow_1 e'\}$, where $e \rightsquigarrow_1 e'$ denotes a directed path with the first and last edges being $e$ and $e'$ respectively, with $\mu(e') = \star$ and any other edge $e''$ has constant weight over time, i.e., $\mu(e'') = 1$;

edges as well as a self-loop that do not have constant weight over time, see case 1 in Figure 1. Then, each of the of the outgoing edges have their dynamics given in terms of a linear combination of the incoming edges, i.e., $\dot{e}_l^+ = w_{l0}e_0 + \sum_{m=1,\ldots,p'} w_{lm}e_m^-$ for $l = 1, \ldots, p$ and $\dot{e}_0 = w_{00}e_0 + \sum_{m=1,\ldots,p'} w_{0m}e_m^-$. If the weight of a self-loop in a vertex $i$ does not vary over time then it is the same as having a vertex without edges from a dynamic point of view, see case 2 in Figure 1. An extension of this scenario is depicted in case 3 in Figure 1, where two vertices $i$ and $j$ are connected by an edge whose weight does not vary over time. In this case, we can understand the total incoming variation of the edge dynamics matching the outgoing variation, hence, the total variation due the incoming edges in vertex $j$ reflects into the outgoing edges' dynamics of vertex $i$. More precisely, we obtain $\dot{e}_l^+ = w_{l0}e_0 + w'_{l0}e'_0 + \sum_{m=1,\ldots,p'} w_{lm}e_m^-$ for $l = 1, \ldots, p$, $\dot{e}_0 = w_{00}e_0 + w'_{l0}e'_0 + \sum_{m=1,\ldots,p'} w_{0m}e_m^-$ and $\dot{e}'_0 = w'_{l0}e'_0 + \sum_{m=1,\ldots,p'} w_{0m}e_m^-$. Further, notice that any graph can be recursively created by a sequence of the previous cases; in particular, if we connect two nodes $i$ and $j$ with outgoing and incoming edges with time varying weights, respectively, through a directed path containing only static nodes and constant weight edges, then it is the same as having the different incoming edges in node $j$ contributing to the dynamics of the outgoing edges in node $i$, see case 4 in Figure 1. Finally, we notice that by specializing the construction to the case where the inputs are considered, it immediately follows that the cost associated to the inputs in the meta digraph is the same as the actuation cost in the dynamic-flow network. ■

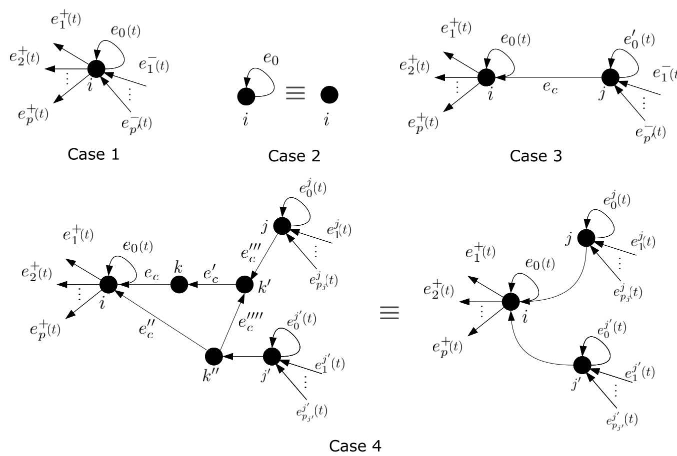


Fig. 1. Cases 1-3 denote the different atomic connections, whereas in Case 4 we can see a composed structure whose interconnections consist of directed paths with constant weight edges and static nodes, i.e., without self-loops.

In addition, it readily follows that the computation complexity of the procedure presented in Algorithm 1 is as follows.

*Theorem 2:* Let $(\mathcal{D} = (\mathcal{V}, \mathcal{E}_{\mathcal{V},\mathcal{V}}), w, \mu, \mathbb{E} = \{E_j\}_{j \in \mathcal{J}}, \mathbb{N} = \{N_i\}_{i \in \mathcal{I}}, \{c_j^E\}_{j \in \mathcal{J}}, \{c_i^N\}_{i \in \mathcal{I}})$ be a dynamic-flow network. Then, Algorithm 1 has polynomial computational complexity given by $\mathcal{O}(|\mathcal{V}| + |\mathcal{E}_{\mathcal{V},\mathcal{V}}|)$. ◇

*Proof:* Step 5 and 7 can be implemented by considering a variation of depth-first search [19]. More precisely, to verify if $e \rightsquigarrow_1 e'$, consider the digraph $\mathcal{D}^\intercal = (\mathcal{V}, \mathcal{E}_{\mathcal{V},\mathcal{V}}^\intercal)$ where the direction of the edges is reversed with respect to $\mathcal{D}$, and perform a depth-first search rooted in $e'$ where adjacency is considered only if the edge has constant weight. If $e$ belongs to such tree, then $e \rightsquigarrow_1 e'$. Similar procedure applies to $e \rightsquigarrow e'$, where after the search has exhausted the constant weight edges, it considers all remaining vertices not in the tree to which a time varying edges connects to. All remaining steps have constant computational complexity; thus, the result follows. ■

Next, we show that the flow-dynamic graphs considered in this paper can lead to an arbitrary meta digraph, once the procedure in Algorithm 1 is used.

*Theorem 3:* The meta digraph $\mathcal{D}^*$ can be an arbitrary digraph. ◇

*Proof:* Suppose that we want to obtain $\mathcal{D}^* = (\mathcal{X}, \mathcal{E}_{\mathcal{X},\mathcal{X}})$, then we just need to consider $\mathcal{D}(\bar{E}) = (\mathcal{W}, \mathcal{E}_{\mathcal{W},\mathcal{W}})$ such that $\mathcal{W} = \mathcal{X} \cup \{e_1, \ldots, e_{|\mathcal{E}_{\mathcal{X},\mathcal{X}}|}\}$, where $\mu(e_i) = 1$ and $\mu(x_j) = \star$ for all $i$ and $j$, respectively. In addition, let $\mathcal{E}_{\mathcal{X},\mathcal{X}} = \{e_1^x, \ldots, e_{|\mathcal{E}_{\mathcal{X},\mathcal{X}}|}^x\}$, and set $e_i$ to be an outgoing edge of $x_j$ and incoming edge in $x_k$ for $e_i^x = (x_k, x_j)$. Then, by executing Algorithm 1 when $(\mathcal{D}(\bar{E}), \mu)$

is considered, we obtain $\mathcal{D}^*$. Figure 2 depicts an illustrative example of the proposed methodology. ■

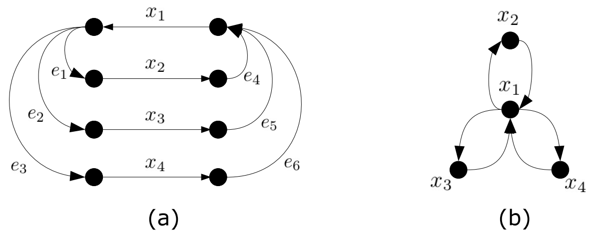


Fig. 2. In this figure, we depict the reduction using Algorithm 1 from the dynamic-flow network in (a) to the meta digraph in (b). In particular, the obtained graph is a 4-vertices star graph which is one of the forbidden subgraphs in a line graph [20], [21].

*Remark 1:* Theorem 3 is relevant to contrast our work with that in [17] where the analysis is done through the line graph $L(\mathcal{G})$, i.e., a graph where the edges of the original graph $\mathcal{G}$ are the vertices of the line graph $L(\mathcal{G})$ and an edge between two vertices exist in $L(\mathcal{G})$ if two edges in $\mathcal{G}$ are incident in the same vertex. In particular, we notice that the line graphs cannot be an arbitrary graph; more specifically, they cannot contain nine *forbidden* subgraphs [20], [21]; in fact, an instance of such forbidden graphs is the 4-star network depicted in Figure 2-(b). ⋄

Next, due to Theorem 3, we can obtain the corollaries stated next.

*Corollary 1:* Determining the minimum cost in-edge inputs can be achieved in $\mathcal{O}(n^\omega)$, where $n$ is the number of state variables in the meta digraph, and $\omega < 2.373$ is the lowest exponent known associated with the complexity of multiplying two $n \times n$ matrices. ⋄

*Proof:* It follows from [10], where a polynomial algorithm, with the aferomentioned computational complexity, to determine the minimum cost of dedicated inputs that ensure structural controllability is proposed. ■

*Corollary 2:* Determining the minimum cost multi-edge and out-node inputs is NP-hard for general dynamic-flow networks. ⋄

*Proof:* The complexity of using multi-edge inputs follows from [12], whereas the complexity of using out-node inputs, i.e., multi-edges inputs that conform with the digraph topology, follows from [22]. ■

Although both the minimum cost multi-edge and out-node inputs problem are NP-hard in general, they are polynomially solvable for a large class of problems, as we obtain in the next result.

*Corollary 3:* If the states of the meta digraph belong to a single strongly connected component, then the minimum cost multi-edge and out-node inputs is polynomially solvable in $\mathcal{O}(n^3)$. ⋄

*Proof:* It follows from [13], where a polynomial algorithm to determine the minimum cost multi-edge and out-node inputs was proposed for strongly connected state digraphs. ■

In the next section, we provide an application of the present framework in terms of modeling time-varying functional connectivity from epileptic human brain. Furthermore, we demonstrate how structural controllability of functional networks can be tested to ensure efficacy of implantable device that target specific brain regions for drug-resistant epilepsy.

## V. A Case Study: Epilepsy-Actuation Schemes

In this section, we ask how structural controllability can be assessed for therapies that actuate neural pathways to treat brain diseases. For instance, assessing structural controllability of epileptic networks is vital for predicting whether implantable devices will be effective at controlling seizures. To demonstrate such an application, we pursue the case-study of a 20 year-old, male undergoing surgical treatment for drug-resistant epilepsy believed to be neocortical origin. As a part of routine clinical workup, the patient underwent implantation of intracranial, subdural electrodes for continuous monitoring of the electrocorticogram (ECoG) to localize regions of the epileptic network responsible for generating seizures. De-identified patient data was retrieved from the online International Epilepsy Electrophysiology Portal (IEEG Portal) [23]. To demonstrate our structural controllability technique, we analyzed data from a patient with 84 intracranially, implanted electrodes and one 107 second long *seizure* (as defined by routine clinical marking). As a control, we also pulled the 107 second interval leading to seizure-onset (referred to as *pre-seizure*).

To test the efficacy of actuating different network regions for seizure control, we first estimated the time-varying functional connectivity of the epileptic network during the pre-seizure period. To measure functional connectivity, we divided the pre-seizure ECoG signal into 1-second, non-overlapping, wide-sense stationary time windows and applied a normalized cross-correlation similarity function between every possible pair of signals. This procedure yields $T$ symmetric, weighted $N \times N$ time-varying adjacency matrices, where $N$ is the number of nodes (ECoG channels) and $T$ is the number of time windows. For our example seizure and pre-seizure data, $T = 107$ and $N = 84$.

Next, we asked which of the strongest functional connections are time-varying or most time-constant during the pre-seizure period. For each unique edge, we measured the average edge strength (Fig. 3) and coefficient of variation (Fig. 4), i.e., the ratio of standard deviation to mean of edge strength, over all $T$ time windows during the pre-seizure period. We retained the 25% strongest edges, of which half the edges with lowest coefficient of variation were considered *time-constant* and with highest coefficient of variation considered *time-varying*, see Fig. 5. The resulting adjacency matrix representing time-constant and time-varying edges is demonstrated in Fig. 6.

Using Algorithm 1, we generate the meta digraph, which describes the dynamics of a given edge in terms of all other interacting edges (Fig. 7), and the control input matrix, which describes the influence of the actuating nodes, in this case chosen as seizure-onset nodes. The control input matrix specifies which state variables in the meta digraph,

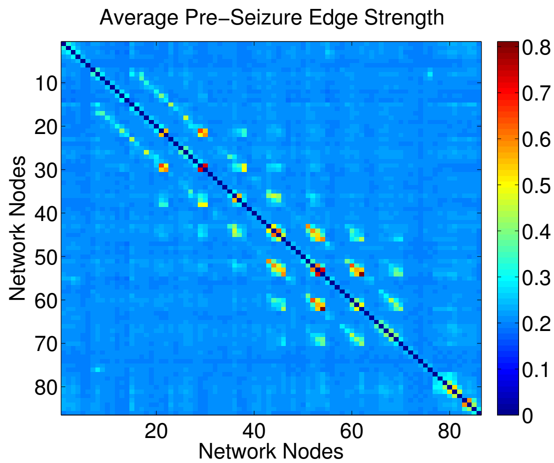


Fig. 3. Average edge strength in dynamic-flow network from 107 time windows preceding seizure onset. Edges strength is the statistical similarity between all possible node (electrode) pairs in the network. Colors represent average edge strength. Clinically-defined seizure-onset nodes are 29 and 37.

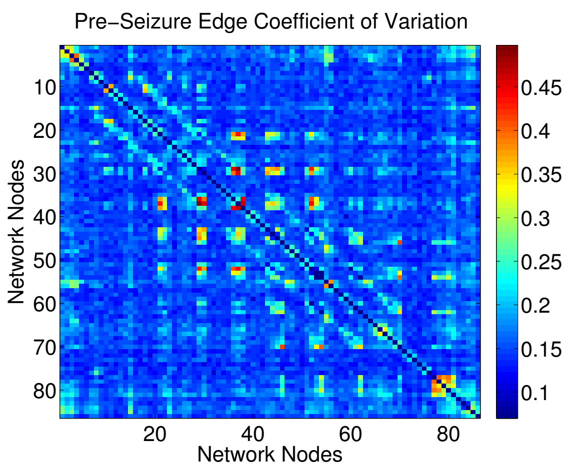


Fig. 4. Coefficient of variation of edge strength in dynamic-flow network from 107 time windows preceding seizure onset. Colors represent the stability of edge strength over time windows.

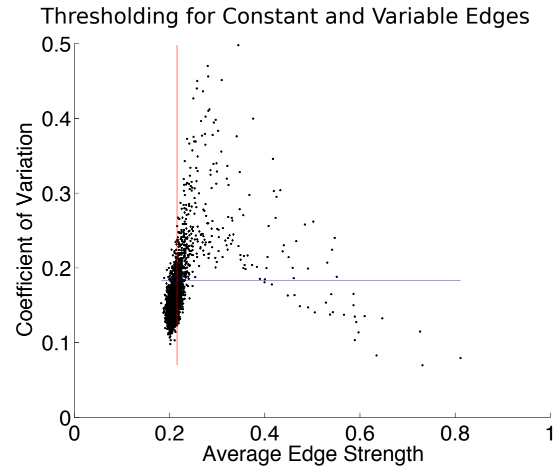


Fig. 5. Relationship between edge strength and coefficient of variation for all edges in the dynamic-flow network. Vertical red line demarcates the threshold used to retain 25% strongest edges. Horizontal blue line is the threshold by which edges with lower coefficient of variation were considered *time-constant* and greater coefficient of variation were considered *time-varying*.

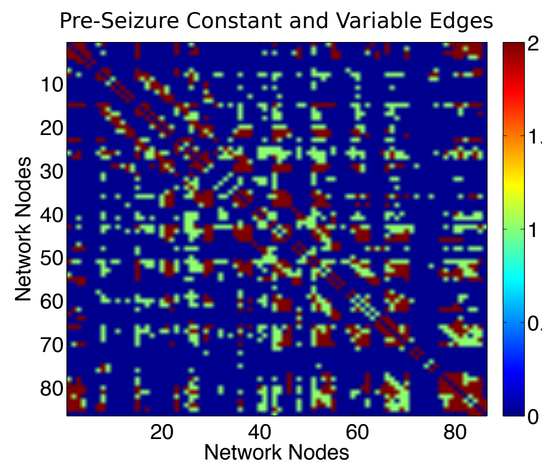


Fig. 6. Adjacency matrix demonstrated edge stability (green) and variability (red).

i.e., the edges in the dynamic-flow network, are actuated. For a point of comparison, we construct the meta digraph under two conditions: (i) real formulation of observed time-constant and time-varying edges; (ii) extreme case where all the strongest edges are considered time-varying, i.e., no time-constant edges exist , as depicted in Fig. 8. We find that the original dynamic-flow network is 4.3% sparse, while the extreme case with strongest edges all considered time-varying is 98.3% sparse. These findings suggest that in the original dynamic-flow, containing some time-constant edges, has greater chance of reaching an edge from any other given edge.

We ask if actuating nodes in the clinically-defined seizure-onset zone ensures structural controllability of the epileptic network. We assume a constant cost of 1 for each in-edge input in the dynamic-flow network, since the regions of interest have similar properties. Using the algorithm implementing Corollary 1 (see [10] for details) with the meta digraph, we find that any single in-edge input within the seizure-onset zone guarantees structural controllability in the epileptic network for the given patient. These results support the capability of current actuating technologies under the assumption that electrode placement captures the full extent of the epileptic region. If we assign different cost to actuating different regions in the epileptic network, due to the dense connectivity (as presented in Fig. 7) any single actuated region will suffice to ensure structural controllability; thus, the less costly, or harmless region should be selected.

## VI. CONCLUSIONS AND FURTHER RESEARCH

In this paper, we have extended the notion of generic controllability for dynamic-flow networks, with either constant and free parameters over time, and provided necessary and sufficient conditions for this to hold. In addition, we address the problem of minimum actuator placement incurring in

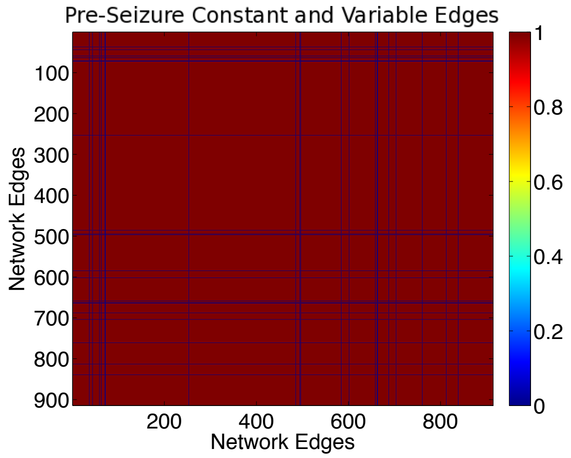


Fig. 7. Meta digraph resulting from a dynamic-flow network with a mixture of time-constant and time-varying edges.

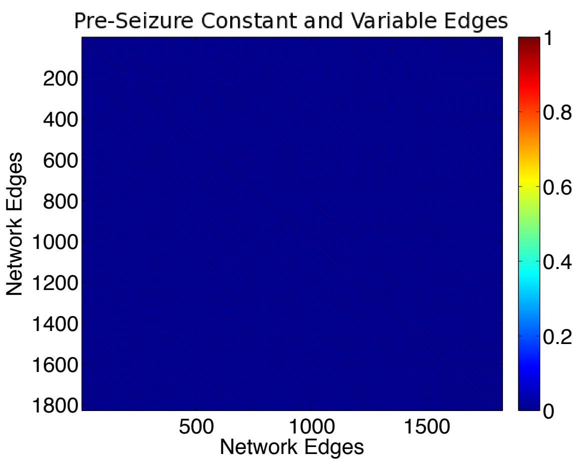


Fig. 8. Meta digraph resulting from a dynamic-flow network when all edges are assumed to be time-varying.

the minimum cost while ensuring structural controllability of the dynamic-flow networks. Finally, we showed how dynamic-flow networks can used as model to identify the regions in the brain that should be actuated to ensure that edges' weights variations are kept within certain bounds. This model allowed us to assess that current actuation capabilities are enough to ensure structural controllability, and determined the location of actuators to regulate the dynamics such that epileptic seizures may be attenuated and/or overcome. We look to pursue model validation in a larger patient cohort as a future line of work. However, applying structural controllability methods to determine optimal actuation schemes at low cost can impact current clinical workflow in placement and configuration of implantable devices.

## REFERENCES


[1] S. Boccaletti, V. Latora, Y. Moreno, M. Chavez, and D.-U. Hwang, "Complex networks : Structure and dynamics," *Phys. Rep.*, vol. 424, no. 4-5, pp. 175–308, Fervier 2006.

[2] D. D. Šiljak, "Dynamic graphs," *Nonlinear Analysis: Hybrid Systems*, vol. 2, no. 2, pp. 544 – 567, 2008, proceedings of the International Conference on Hybrid Systems and Applications, Lafayette, LA, USA, May 2006: Part II.

[3] R. M. Hutchison, T. Womelsdorf, E. A. Allen, P. A. Bandettini, V. D. Calhoun, M. Corbetta, S. D. Penna, J. H. Duyn, G. H. Glover, J. Gonzalez-Castillo, D. A. Handwerker, S. Keilholz, V. Kiviniemi, D. A. Leopold, F. de Pasquale, O. Sporns, M. Walter, and C. Chang, "Dynamic functional connectivity: Promise, issues, and interpretations," *NeuroImage*, vol. 80, 10 2013.

[4] A. Zecevic and D. D. Šiljak, "Control of dynamic graphs," *SICE Journal of Control, Measurement, and System Integration*, vol. 3, no. 1, pp. 1–9, 2010.

[5] J.-M. Dion, C. Commault, and J. V. der Woude, "Generic properties and control of linear structured systems: a survey." *Automatica*, pp. 1125–1144, 2003.

[6] L. Markus and E. B. Lee, "On the existence of optimal controls," *Journal of Basic Engineering*, vol. 84, no. 1, pp. 13–20, 1962.

[7] X. Liu, H. Lin, and B. M. Chen, "Structural controllability of switched linear systems," *Automatica*, vol. 49, no. 12, pp. 3531 – 3537, 2013.

[8] S. Pequito, S. Kar, and A. Aguiar, "A structured systems approach for optimal actuator-sensor placement in linear time-invariant systems," *Proceedings of American Control Conference (ACC)*, pp. 6108–6113, June 2013.

[9] S. Pequito, S. Kar, and A. P. Aguiar, "A framework for structural input/output and control configuration selection of large-scale systems," *IEEE Transactions on Automatic Control*, vol. 61, no. 2, pp. 303–318, Feb 2016.

[10] S. Pequito, A. P. Aguiar, and S. Kar, "Minimum Cost Structural Input/Output Selection for Large-Scale Linear Time-Invariant Systems," *To appear in Automatica*, Mar. 2016.

[11] S. Pequito, J. Svacha, G. J. Pappas, and V. Kumar, "Sparsest minimum multiple-cost structural leader selection," *IFAC-PapersOnLine*, vol. 48, no. 22, pp. 144 – 149, September 2015, 5th IFAC Workshop on Distributed Estimation and Control in Networked Systems (NecSys).

[12] S. Pequito, S. Kar, and A. P. Aguiar, "On the complexity of the constrained input selection problem for structural linear systems," *Automatica*, vol. 62, pp. 193 – 199, 2015.

[13] S. Pequito, S. Kar, and G. Pappas, "Minimum cost constrained input-output and control configuration co-design problem: A structural systems approach," in *Proceedings of the American Control Conference (ACC)*, July 2015, pp. 4099–4105.

[14] S. Pequito, P. Bogdan, and G. J. Pappas, "Minimum Number of Probes for Brain Dynamics Observability," *Proceedings of the 54th Conference on Decision and Control 2015*, pp. 306–311, Dec. 2015.

[15] S. Pequito and G. J. Pappas, "Structural Minimum Controllability Problem for Linear Continuous-Time Switching Systems," *Under Review*, Jul. 2015. [Online]. Available: http://arxiv.org/pdf/1507.07207v1

[16] G. Ramos, S. Pequito, A. Aguiar, J. Ramos, and S. Kar, "A model checking framework for linear time invariant switching systems using structural systems analysis," in *51st Annual Allerton Conference on Communication, Control, and Computing (Allerton)*, Oct 2013, pp. 973–980.

[17] T. Nepusz and T. Vicsek, "Controlling edge dynamics in complex networks," *Nat Phys*, vol. 8, no. 7, pp. 568–573, Jul. 2012.

[18] M. R. Garey and D. S. Johnson, *Computers and Intractability: A Guide to the Theory of NP-Completeness*. New York, NY, USA: W. H. Freeman & Co., 1979.

[19] T. H. Cormen, C. Stein, R. L. Rivest, and C. E. Leiserson, *Introduction to Algorithms*, 2nd ed. McGraw-Hill Higher Education, 2001.

[20] A. van Rooij and H. Wilf, "The interchange graph of a finite graph," *Acta Mathematica Academiae Scientiarum Hungarica*, vol. 16, no. 3-4, pp. 263–269, 1965.

[21] D. B. West, *Introduction to Graph Theory*, P. Hall, Ed. Prentice Hall, 2001.

[22] S. Pequito, S. Kar, and A. Aguiar, "Minimum number of information gatherers to ensure full observability of a dynamic social network: A structural systems approach," in *2014 IEEE Global Conference on Signal and Information Processing (GlobalSIP)*, Dec 2014, pp. 750–753.

[23] J. Wagenaar, B. Brinkmann, Z. Ives, G. Worrell, and B. Litt, "A multimodal platform for cloud-based collaborative research," in *Neural Engineering (NER), 2013 6th International IEEE/EMBS Conference on*, Nov 2013, pp. 1386–1389.