A Fractional-Order MPC Framework for Electrical Neurostimulation in Epilepsy

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I. Introduction: Electrical Neurostimulation

In the context of healthcare applications, cyber-physical systems (CPSs) bring the promise of enabling a continuous and automatic monitoring and interaction of subjects, with the objective of ensuring or enhancing their quality of life. As a consequence, CPSs possess the potential to lower healthcare costs for prevention and therapies associated with chronic diseases (e.g., heart diseases, diabetes, and neurological disorders and diseases such as epilepsy, Alzheimer's, and Parkinson's). *Electrical neurostimulation* is an increasingly adopted therapeutic methodology for neurological conditions such as epilepsy [1], as well as Alzheimer's, Parkinson's, depression, and anxiety, just to mention a few. Devices designed to conduct such stimulation, particularly implantable ones, are commonly characterized by their limited sensing, actuating, and computational capabilities. However, the sensing mechanisms are often used only for their detection potential (e.g., to detect seizures), which automatically and dynamically trigger the actuation capabilities, but ultimately deploy prespecified stimulation doses that resulted from a period of manual calibration. The potential information contained in the measurements acquired by the sensing mechanisms is, therefore, considerably underutilized, given that this type of stimulation strategy only entails an event-triggered relationship between the sensors and actuators of the device. Such stimulation strategies are suboptimal in general and lack theoretical guarantees regarding their performance.

II. Linear Fractional-Order Systems (FOS)

In the context of neurophysiological signals, temporal *fractional* properties in both health and disease states have become apparent and with a huge potential for clinical applications [2]. Geometrically, such properties entail self-similarity of signals at different time scales. Practically, this leads signals to become non-stationary and to possess long-term memory dependencies with themselves, with the backwards-decaying weights of such dependencies following a power-law distribution. Nonetheless, only recently have dynamical *spatiotemporal* fractional models been proposed as a tool to model neurophysiological signals suitable to deal with structured data and to equip us with modeling capabilities that capture both a *spatial* aspect (i.e., the contributions of the signal's components into each other) and *temporal* long-range memory associated with the power-law exponents. More precisely, denote the vector signal $x_k \in \mathbb{R}^n$ that lumps together the n measured brain signals of an epileptic patient at a discrete time step k (i.e., at time $t_k = k\Delta t$) through electrodes integrated in an implantable neurostimulator. Then, we will consider a linear *fractional-order system* (FOS) model

$$\Delta^\alpha x_{k+1} = Ax_k + Bu_k, \tag{1}$$

for the evolution of this neurophysiological signals, where the *state matrix* A captures the spational component previously described, and the vector of *fractional-order coefficients* $\alpha = (\alpha_1, \ldots, \alpha_n)$ captures the *temporal* relationship. The operator Δ^α is referred to as the *Grünwald-Letnikov difference operator* of (fractional) order α, and is such that (1) can be written as

$$x_{k+1} = \sum_{j=0}^{k} A_j x_{k-j} + Bu_k \tag{2}$$

with A_0 being a function of (A, α), and the the remaining A_j's functions of α decaying in j. Finally, the exogenous input vector u_k represents the neurostimulator's electrical stimulus signal. We will now propose a control design strategy for u_k so as to automatically attempt to drive the state x_k towards a range of normal brain activity, whenever an ictal period naturally starts to take place.

III. Model Predictive Control (MPC)

Model-based approaches allow us to predict and understand how an external signal or stimulus would craft the dynamics of the process, which we can leverage for the desired control law design. That said, due to the highly dynamical nature of the neurophysiological processes, it is imperative that we consider true *feedback* mechanisms (as opposed to open-loop or event-triggered open-loop ones) by leveraging the continuous flow of measurements of the system to automatically regulate the control signal. *Model predictive control* (MPC) [3] entails a strategy that leverages a model's predictive capability together with a feedback relationship to accommodate for system-model mismatch and/or model uncertainty. More precisely, the feedback comes in the form of frequently optimizing an cost functional that encapsulates the risk assessment of abnormal behavior over a receding finite horizon, which serves as a short-term predicted sequence of optimal control inputs, which will be revised at or before the short term's completion.

IV. An MPC-FOS Strategy for Epileptic Seizure Mitigation

Combining all the ingredients discussed so far, we propose an MPC strategy for the electrical neurostimulation signal of an implantable device, so as to mitigate or abort seizures. The proposed predictive model is based on a (truncated) FOS model, due to the ability of fractional-order dynamics to more accurately capture the long-term dependence present in biological systems, as compared to the standard linear time-invariant models.

To establish the potential of our framework, we focus on epileptic seizure mitigation by computational simulation of our proposed strategy upon seizure-like events. First, we identified the parameters A and α in (1) that fit an excerpt from PhysioNet's *CHB-MIT Scalp EEG Database* available at https://physionet.org/pn6/chbmit/. Then, we implemented our proposed novel stimulation strategy described earlier. We used a simple quadratic cost functional that measures the brain signals overall energy, plus a regularization term based on the overall input energy spent. Furthermore, safety-related range constraints were used for the input, which are linear, and thus the associated finite-horizon optimal control problem entails only a quadratic program (QP) that can be efficiently solved by numerical means. Other MPC-related parameters such as the prediction and control horizons, as well as the finite-history horizon for the approximation of the identified FOS model as a multivariate autoregressive model were obtained empirically. More research will be conducted to formally understand the tradeoffs between these so as to help guide its implementation.

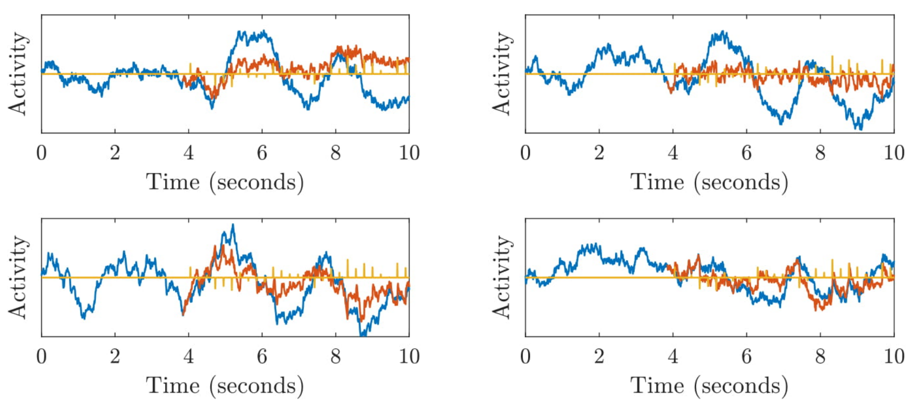

Fig. 1. Simulated seizure-like event is depicted in blue over 4 joint electrode channels during a 10sec window. The controlled signals, under our stimulation strategy, are depicted in red. The electrical stimulation signal, manually deactivated before the 4sec mark, is depicted in yellow.

The results are presented in Fig. 1 include 4 channels controlled simultaneously, since failure to drive any one of them towards a normal range would imply failure in the overall seizure mitigation objective. We can see that the proposed stimulation strategy achieves the desired goal and implicitly provides us with a detector, given that it tends to provide virtually no stimulation except during very briefs periods of times, at which point only (time-varying) impulse-like stimuli are deployed.

References

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