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A data-driven model inversion approach to cancer immunotherapy control

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Abstract— **A novel data-driven control design approach for Multiple Input Multiple Output nonlinear systems is proposed in the paper, relying on the identification of a polynomial prediction model of the system to control and its on-line inversion. A simulated study is then presented, concerning the design of a control strategy for cancer immunotherapy. This study shows that the proposed approach may be quite effective in treating cancer patients, and may give results similar to (or perhaps better than) those provided by "standard" methods. The fundamental difference is that "standard" methods are typically based on the unrealistic assumption that an accurate physiological model of the cancer-immune mechanism is available; in the approach proposed here, the controller is designed without such a strong assumption.**

I. Introduction

Standard approaches to control are based on first-principle models: they assume that an accurate physical model describing the dynamics of the system to control is available. Typical examples are feedback linearization [14], Lyapunov function based control [20] and NMPC (Nonlinear Model Predictive Control) [1], [2]. However, in many real-world applications, deriving an accurate model is an extremely difficult task, since the system dynamics is often not well known and/or too complex. Robust methods might be used to deal with this problem, [12], [29]. However, deriving the necessary uncertainty models is not an easy task even for LTI (Linear Time Invariant) systems (see e.g. [7] and the references therein), and is a largely open problem in the case of nonlinear systems. Another relevant issue is that, in the case of nonlinear system, even when a reliable model is available, designing a (nonlinear) controller is in general difficult.

Data-driven methods have been introduced to cope with these problems, see, e.g., [19], [6], [5], [10], [3], [24], [16]. Several of these approaches are also described in [21], with useful discussions on their practical advantages and drawbacks. However, guaranteeing general a-priori stability and accuracy properties is not easy for many data-driven methods. Typically, the controller is first designed using some heuristic or some more systematic technique, then it is tested/tuned in simulation, and finally it is implemented (and possibly tuned) on the real plant to control. Another issue is that many data-driven methods are based on neural networks or similar approximating functions, whose design involves non-convex optimization in large dimensional spaces. There is thus no guarantee that the resulting controller is adequate to solve the control problem.

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In this paper, a novel data-driven control method for general MIMO nonlinear systems is proposed, called Nonlinear Inversion Control (NIC), allowing us to overcome all these relevant problems: the method does not require a physical model of the plant to control; it can guarantee a priori important properties such as closed-loop stability and tracking error accuracy; it is relatively simple; it is systematic, in the sense that the design parameters can be chosen by means of a precise procedure; it is numerically efficient, allowing a "fast" implementation on real-time processors. The NIC method is based on the identification from data of a polynomial prediction model and its online inversion through efficient optimization algorithms. An important point is that closed-loop stability is directly enforced by the identification algorithm used to derive the model, thus avoiding the need of additional on-line operations finalized at stabilization (as typically done in NMPC). A SISO version of the NIC approach can be found in [11], [27].

Thanks to these features, the NIC approach may be particularly effective in therapy control, where typically there is a huge variability among the patient population and, moreover, it is extremely difficult to derive accurate physiological models. The NIC approach allows indeed the design of therapy control strategies that are personalized for each patient, avoiding the population variability problem. Also, it does not require accurate physiological models: control design is carried out from a set of data acquired in a preliminary phase of the therapy.

A simulated study is presented, concerning the design of a control strategy for cancer immunotherapy, based on interleukin, a type of proteins that help the immune system to produce cells which can defeat cancer. This study shows that the proposed approach may be quite effective in treating cancer patients, giving results similar to (or perhaps slightly better than) those provided by a "standard" method. The fundamental difference is that this "standard" method is based on the unrealistic assumption that an accurate physiological model of the cancer-immune mechanism is available; in the NIC approach, the controller is designed without using such a strong information.

II. Problem formulation

Consider a MIMO (Multiple Input Multiple Output) nonlinear discrete-time system of the form

$$y_t = h\left(u_t^-, y_t^-, \xi_t^-\right) \tag{1}$$

$$\begin{aligned} u_t^- &\doteq (u_{t-1}, \ldots, u_{t-n}) \\ y_t^- &\doteq (y_{t-1}, \ldots, y_{t-n}) \\ \xi_t^- &\doteq (\xi_{t-1}, \ldots, \xi_{t-n}) \end{aligned}$$

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