Foreword Identification and Control in Biomedical Applications

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Published in:
IEEE Transactions on Control Systems Technology

DOI:
10.1109/TCST.2019.2957597

Foreword
Identification and Control in Biomedical Applications

CONTROL engineering (in the broad sense of the term) has become an important enabling technology in many areas of medicine. Prominent examples include the artificial pancreas, closed-loop anesthesia, and personalized drug dosing strategies in neurology, oncology, endocrinology, and psychiatry. It is a testament to the power of control systems that allow individualizing treatment by providing mechanisms for linking treatment goals to treatment regimens, thus achieving a desired therapeutic effect. Consequently, the arrival of control systems engineering to the clinic enables the visionary concept of "treat the patient, not the disease" technologically and economically feasible.

This Special Issue is a joint effort of the three IEEE Control Systems Society Technical Committees: System Identification and Adaptive Control, Systems Biology, and Healthcare and Medical Systems. It addresses the challenges of applying feedback/feedforward control and related technologies in living organisms, with an emphasis on biomedicine. Mathematical models of systems in the human body can be used to uncover and quantify dynamical contributions to health and disease. The insights obtained are expected to be instrumental in the design of innovative and agile tools for modeling, analysis, design, and optimization of biomedical systems.

Altogether, 22 articles are included in this Special Issue and cover a wide field within biomedicine and behavioral medicine, thus reflecting a diversity of topics where control and dynamical systems' modeling have an important role. Mathematically, describing and controlling metabolic activity is a popular research area motivated by the need to understand the dynamics of metabolism and thus to improve the treatment of chronic conditions, such as diabetes. Applications to neuroscience and neurology are gaining increasing acceptance, given the rise of research initiatives in America and Europe targeting the human brain, as well as the increasing prevalence of neurological disorders in the world's population. Articles in the issue address a diversity of illnesses, conditions, and treatments (e.g., Type 1 and Type 2 diabetes, Parkinson's disease, deep brain stimulation, myocardial infarction, influenza and epidemic disease treatment, tumor therapy, weight control, neuromodulation, muscular rehabilitation, physical activity, and behavioral medicine), control strategies (e.g., feedback, feedforward, model predictive, nonlinear, data-centric/data-driven, and impulsive), and modeling/estimation approaches (e.g., fractional models, Markov models, prediction-error estimation, semiphysical identification, and Kalman filtering). The preponderance of the approaches considered in this Special Issue is tested either with clinical data or via rigorous simulation.

This Special Issue is spearheaded by articles devoted to metabolic illnesses, artificial pancreas, and glucose control, addressing both Type 1 and Type 2 diabetes. Yu *et al.* study the problem of glucose prediction using sparse kernel filtering algorithms. Computationally efficient adaptive and recursive filtering algorithms are developed to provide online predictions of blood glucose in patients with Type 1 diabetes. Di Ferdinando *et al.* describe a nonlinear sampled-data feedback controller for the glucose–insulin system meaningful for Type 2 diabetes. While less severe than Type 1, Type 2 diabetes is more prevalent. Data-driven anomaly recognition for model-free fault detection is the focus of Meneghetti *et al.*'s work, while data-driven disturbance estimation and control applied to glucose regulation is the primary emphasis of the work by Novara *et al*. The section is rounded out by the work of Guo *et al.* in examining the problem of estimating energy intake (essential to weight control and understanding metabolic function), which is studied in the context of weight gain in pregnancy for an overweight/obese population.

Three articles address issues with modeling and control of infectious diseases. The article by Paré *et al.* presents a rigorous analysis of spreading models on nontrivial networks. Several models in the literature are compared, and one is studied analytically, along with two real-world data sets that are used to validate one well-known approximation of the susceptible-infected-susceptible model. A discrete-time inverse optimal impulsive control scheme is proposed by Hernandez Mejia *et al.* in the second article to address the antiviral treatment scheduling problem. The authors develop a model whose parameters are tuned using data from clinical trials and present results supporting the effectiveness and robustness of the proposed optimal antiviral treatment schedule. The article by Cacace *et al.* develops a novel optimal control algorithm applied to the design of a feedback antiangiogenic tumor therapy. Lack of data is mitigated by the use of a state observer that exploits recent measurements. The algorithm is validated on a virtual population through a rigorous set of simulations.

Neuroscience and neurological efforts are featured in four articles. These include the work of Olsson and Medvedev on nonparametric tremor quantification with smartphones; the approach leads to significant improvements compared with

Digital Object Identifier 10.1109/TCST.2019.2957597

standard spectral analysis. Fractional-order modeling for a so-called "phantom" electroencephalographic (EEG) system is examined in the work of Besancon *et al.*, which can be used as a support to analyze dynamical behaviors in standard EEG measurement processes. Shakarami *et al.* rely on novel formulations of the Kalman filter for intraoperative brain shift estimation using atlas of brain deformations. Finally, Cubo and Medvedev examine online tissue conductivity estimation in the context of deep brain tissue stimulation, a therapy used for alleviating symptoms associated with Parkinson's disease.

Cardiac and respiratory illnesses represent the next group of articles. The work of Hunnekens *et al.* discusses a variable-gain control strategy for mechanical ventilators in respiratory systems. System identification using fractional models is again examined in this issue, in the article by Victor *et al.*, as an approach to modeling thermal transfer in the lungs. Meanwhile, a mechanistic framework sets the underpinnings for modeling and system identification of biomarkers that are released during acute mycardial infarction, as described in the work in Procopio *et al.*; this work is the first (to the best of our knowledge) to account for the dynamics of cardiac biomarker release.

Two articles form part of the section on systems biology. This includes the work by Bianconi *et al.* on cancer systems biology, who present an innovative Bayesian method called conditional robust calibration (CRC) for model calibration and identifiability analysis in this problem space. Multiobjective system identification of a feedback synthetic gene circuit, a highly nonlinear, stochastic problem, is examined by Boada *et al*. Two articles, meanwhile, are associated with muscular applications. van de Ruit *et al.* rely on both nonparametric and parametric kernel-based regression to monitor time-varying joint impedance during a force task; the approaches yield complementary insights. The work by Paz *et al.* uses stochastic extremum seeking to adapt the gains of a PID control law for functional neuromuscular electrical stimulation.

A final group of articles considers closed-loop anesthesia, physical activity, and behavior change. The article by van Heusden *et al.* uses multi-input single-output (MISO) closed-loop identification to take the response to disturbances during induction of anesthesia into account. From this approach, the authors identify and validate several models that describe the blood pressure and the depth-of-hypnosis response to propofol infusion for patients at risk of cardiovascular suppression. The article by Lopes dos Santos *et al.* reformulates and adapts a class of identification algorithms known as matchable-observable linear identification (MOLI) to estimate linear time-invariant models for *Just Walk*, a behavioral intervention designed on the basis of system identification principles to increase physical activity in sedentary adults. These results provide insights into the individual and the intervention, which can be used to improve the design of future studies. The final article in this Special Issue is focused on social cognitive theory (SCT), an important theory meaningful in many application settings, including the health behavior. Martin *et al.* postulate a dynamical systems model for SCT that can be used to predict changes in health behavior over time and can be validated through "intensive" data streams generated by wearables and related devices that form an increasing part of mobile health (mHealth). These models, in turn, can lead to novel forms of optimized interventions based on control systems' engineering principles.

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