Guest Editors' Introduction: Cyber–Physical Systems for Medical Applications

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■ **It is our** pleasure to introduce this special issue on Cyber–Physical Systems for Medical Applications. With the deeper integration of computation, communication, and control of electronics and software in medical devices, we are faced with new challenges on design and test of systems with the patient-in-the-loop. For biological and medical domains, the operating environment encompasses a rich web of genomic (transcription, translation, splicing), metabolic (anabolic or catabolic reactions), and physiologic (e.g., heart rate variability, blood glucose dynamics, brain activity) processes that exhibit irregular and time-dependent behavior that is not amenable to simplified models.

This brings about significant challenges in the modeling, testing, verification, and design of medical systems. For instance, from 1990 to 2000, 600 000 pacemakers were recalled and over 40% were due to software/firmware issues. Similar efforts are sustained for developing artificial pancreas that can maintain the blood glucose within safe bounds with minimal interventions throughout daily activities. As patient dynamics are nonlinear, often nondeterministic, and depend on several environmental, genetic, and physiological contexts, there is a need for both formal and functional modeling to better understand interactions with invasive care.

To meet the safety and efficacy requirements including responsiveness, reliable operation, low power, and secure delivery of therapy, there is an urgent need for a new science of cyber-physical system (CPS) design where device-patient interaction modeling and testing are at the core of any optimization. Several such challenges across low-power data acquisition, long-life implantable system design, high throughput tissue-electrode interfaces, wearable flexible electronic substrates, electrical modulation for physiological response, robotic surgery, clinical process modeling, and complex analysis of infections are actively pursued across research communities.

This special issue highlights recent investigations regarding various challenging problems we face in medical CPSs. The selected papers represent both theoretical and system perspectives in medical CPSs.

"Parameter-invariant design of medical alarms," by Weimer et al. tackles an important challenge in medical CPSs—the control of structured dynamics with unknown parameters—and presents a design methodology for medical parameter-invariant monitors. Along the same lines, Silva et al. in "Modeling the effect of intravenous anesthetics: A path toward individualization" review the challenges presented by the complex phamocokinetic/pharmacodynamics models and advocates for the adoption of models with reduced complexity for individualized closed-loop controllers used in automated drug delivery. Besides modeling and control, an important issue in medical CPSs is related to the design, testing, and certification methodologies. Huang et al. in "Simulation-based verification of cardiac pacemakers with guaranteed coverage" provide an overview of the simulation-based verification techniques to ensure guaranteed

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coverage for nonlinear hybrid systems and describe a formalism based on discrepancy functions for investigating the time-bounded safety of pacemakers. The proposed formalism is showcased for a family of pacemaker designs in order to demonstrate strategies for determining the safe parameter ranges. Medical CPSs are expected not only to provide a more appropriate control of human physiology, but also to enable a significant improvement in care for adults with special needs. In "Caring analytics for adults with special needs," Wolf et al. propose a caring analytics approach that collects and mines heterogeneous sensor network data for identifying the actions that should be taken for improving the care and quality of life of adults with special needs.

Regulatory issues of medical device software and their certification are a challenge as we may not be able to fully model the physiological but must still guarantee the closed-loop safety and efficacy of the interacting device. To address this, "Can product-specific assurance case templates be used as medical device standards?" by Wassyng et al. provides a systematic approach for semiformal reasoning with structured assurance cases for different device and interaction types. This is complemented by Ray et al., in "Security assurance cases for medical cyber–physical systems," which make security extensions to assurance cases. As medical devices evolve and grow in complexity, it is necessary to ensure that new and modified operating modes still maintain the safety that existed in prior iterations. To address this, Murugesan et al. in "Design considerations for modeling modes in cyber-physical systems" propose a generic pattern to structure the mode logic such that additions, modifications, and removal of behaviors could be done in a quick and localized fashion without losing model integrity. Another important dimension in medical CPSs is represented by their increasing size and complexity, which brings into question the compositionality challenge. To this end, Larson et al. describe in "Enabling safe interoperation by medical device virtual integration" a framework for constructing safe interoperating medical device systems.

The rapid emergence of medical telerobotics has brought about several unanticipated safety and reliability challenges in physician training, machine-human feedback, and faults during operation. To address this, Kumar et al. survey the benefits of computer vision for preoperative, intraoperative, and postoperative surgical stages in "Computer-vision-based decision support in surgical robotics." Similarly, for medical capsule robots used as diagnostics and interventional tools, in "Systematic design of medical capsule robots," Beccani et al. present an early effort for an open architecture, platform design, software infrastructure, and a supporting modular design environment.

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