Simulation-Based Test and Validation of Medical Cyber-Physical Systems for Critical and Perioperative Care

Extended Abstract†

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1 INTRODUCTION

Managing physiology in critical and perioperative settings requires the closed-loop process of monitoring patient state, and deciding on and applying appropriate interventions (including inaction). This typically involves clinicians manually operating medical devices while making complex decisions. A desirable alternative is what we term Closed Loop Assistants (CLAs), computing devices that assist clinicians by evaluating parameters obtained from monitoring devices, and when appropriate, automatically executing changes to infusion pump parameters under a clinician's supervisory control. This allows the clinician to attend to the overall situation and setting of targets, while being relieved from making many manual device adjustments.

During the development of any closed-loop system, it is important to validate ideas early and often. The more realistic the environment the system can be tested in during this stage, the better the early concept designs and the resulting final design. The traditional approach for providing realistic environments for medical systems is to use animal models in pre-clinical trials. This is expensive and lacks control over the environment (animal) and repeatability of experiments. Human trials provide a more realistic environment, but with the same issues of expense and repeatability. The use of *in silico* patients, computer models of patient physiology, allow extensive, repeatable evaluation of physiological responses to CLAs not achievable with biological systems at any price. This approach has been advocated for in the vision for emerging medical technologies like CLAs [1] and have been successfully used in the design of other technologies like pacemakers [2] and diabetes management systems [3]. In the diabetes case, the FDA accepts test with these *in silico* patients as an alternative to animal trials. The CLA case represents more complex physiologic interactions than the previous two cases. In addition, the CLA must operate as a tool in the clinician's toolbox, much like any medical device, so designers must be able to also evaluate the CLA-clinician interaction to ensure that this results in maximum synergy and the best possible outcome for patients.

We have been developing a framework for simulation-based testing of CLAs for critical and perioperative care. Our framework allows both software-only simulations, which yield quicker results at reduced realism, as well as full, real-time system-in-the-loop simulations where *in silico* patients interact in real-time with a realistic CLA [4] that leverages real medical devices, yielding slower results but at increased realism. We have applied this framework to a simple case study of hypotension management on a small *in silico* patient population. The results show trends that can be gleaned about the behavior of the system as its environment (the patients) and its parameters vary.

2 THE FRAMEWORK

The framework consists of two pieces, the *in silico* patients and the CLA portion. A current limitation of the real-time portion of our framework is that the pump is not directly connected to the *in silico* patients. Rather, we intercept the messages between the control algorithm and the pump and pass this to the *in silico* patient simulation. We are working on a solution where the pump is connected to the simulation directly, which would make our *in silico* patient simulation part of the framework fully agnostic the medical devices it interacts with. It is currently agnostic to the patient monitor.

A key feature of this framework is that it allows for exploration of the behavior of the system across different patients. This is important for determining and improving the robustness of the system to interpatient variation. All simulations are instrumented and the system is time-synchronized to ensure that events overtime across the system can be captured and analyzed. This allows us to both examine how the system affects the patient and how the behavior of this system (internally) is affected by the current patient physiology and other current conditions.

3 CASE STUDY

We have validated this framework on simple case stated based on a realistic scenario of hypotension management that occurs in the ICU. The control algorithm is a simple control to range algorithm based on the way clinicians currently manage hypotension. The goal of the case study was not to develop an optimal algorithm, but to illustrate the kinds of the explorations that the framework allows. We run the case study on all three different instantiations of the framework (pure

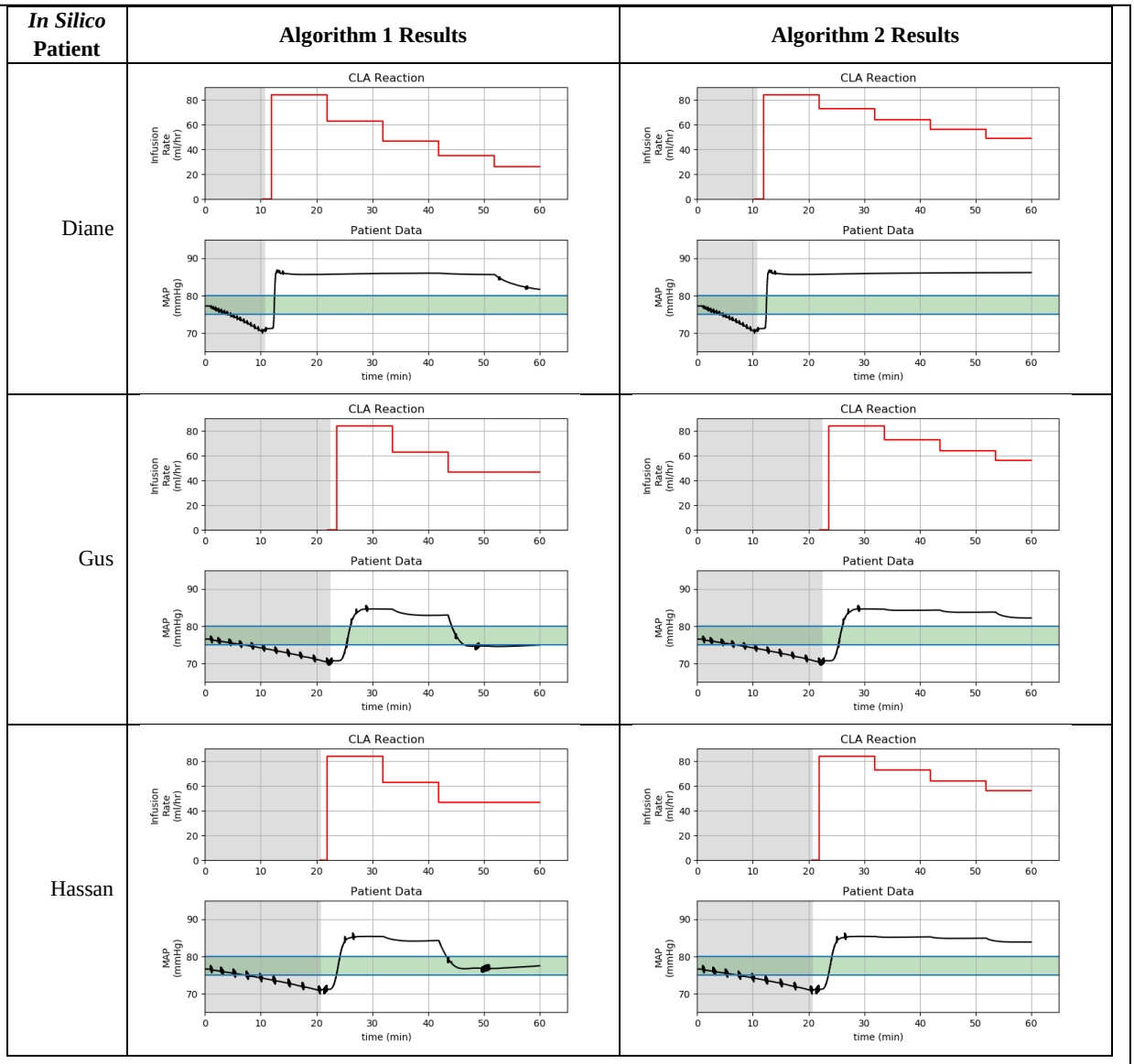

Figure 1. Results of pure simulation of case study on three *in silico* patients with two different versions of an algorithm.

simulation to real-time with real devices). The results for both algorithms across three patients is shown in Figure 1. The real-time simulation produces similar results. There was a discrepancy between pure software and real-time results in one case, but the details provided by the framework allowed use to understand how this arose.

4 DISCUSSION AND FUTURE DIRECTIONS

Our work demonstrates a proof-of-concept for simulation-based testing of medical cyber-physical systems for critical and perioperative care. Our future work includes expanding the patient population to have more variability and to improve patient physiology to mimic surgery and ICU cases. We are also looking to incorporate formal methods and verification techniques to complement our simulation-based approaches.

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