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In Silico Preclinical Trials: Methodology and Engineering Guide to Closed-Loop Control in Type 1 Diabetes Mellitus

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Abstract

This article sets forth guidelines for *in silico* (simulation-based) proof-of-concept testing of artificial pancreas control algorithms. The goal was to design a test procedure that can facilitate regulatory approval [e.g., Food and Drug Administration Investigational Device Exemption] for General Clinical Research Center experiments without preliminary testing on animals. The methodology is designed around a software package, based on a recent meal simulation model of the glucose–insulin system. Putting a premium on generality, this document starts by specifying a generic, rather abstract, meta-algorithm for control. The meta-algorithm has two main components: (1) patient assessment and tuning of control parameters, i.e., algorithmic processes for collection and processing patient data prior to closed-loop operation, and (2) controller warm-up and run-time operation, i.e., algorithmic processes for initializing controller states and managing blood glucose. The simulation-based testing methodology is designed to reveal the conceptual/mathematical operation of both main components, as applied to a large population of *in silico* patients with type 1 diabetes mellitus.

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Abbreviations: (ARX) autoregressive, external input, (BG) blood glucose [concentration], (CGM) continuous glucose monitoring/monitor, (CHO) carbohydrate, (CVGA) control variability grid analysis, (FDA) Food and Drug Administration, (GCRC) General Clinical Research Center, (ICU) intensive care unit, (IDE) Investigational Device Exemption, (JCHR) Jaeb Center for Health Research, (JDRF) Juvenile Diabetes Research Foundation, (LBGI) low blood glucose index, (MPC) Model Predictive Control, (SD) standard deviation, (T1DM) type 1 diabetes mellitus, (UVA) University of Virginia

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