Control Subject to Human Behavioral Disturbances: Anticipating Behavioral Influences in the Control of Diabetes (CNS-0931633) Stephen D. Patek (PI), School of Engineering and Applied Science, University of Virginia

This project addresses the design of cyber-physical systems that respond to behavioral disturbances introduced by human users. The primary motivating example of this research is the design of "artificial pancreas" algorithms for the control of blood glucose in patients with Type 1 diabetes who require external insulin throughout the day to maintain glucose homeostasis. Whereas individual patients have their own preferences with regard to the degree of automation needed (with some desiring fully automatic delivery of insulin, others wanting only advice), the control problem itself is largely defined in terms of the uncertainties associated with daily activities: meals and exercise.

From recent clinical studies of fully automated control of diabetes, it is clear that deterministic model predictive methods can effectively deal with the measurement and actuation delays associated with current-generation continuous glucose monitors and insulin pumps. However, it is also clear that outside of the controlled environment of a clinical research center it is necessary to make special accommodations for spurious human behavioral disturbances. Specifically, (i) system disturbances, such as meals and exercise, may have to be announced by the patient (requiring an intrusion upon the patient's lifestyle), (ii) it may be necessary to integrate specialized algorithms for detecting meals and exercise (which are prone to errors and introduce delay), and/or (iii) the system may need to be de-tuned so that unannounced meals and exercise can be safely absorbed by the system.

In this work, we take the view that stochastic methods can play a significant role in bridging the gap between model predictive control and uncertain system disturbances caused by human behavior. In particular, we assert that many system disturbances can be modeled (i) as random processes, but not as zero-mean white noise processes, and (ii) as occurring with statistical regularity, but not as periodic. Accordingly, we are developing new mathematical models of human behavioral disturbances. Our premise is that appropriate statistical characterizations of routine behavior allow us to derive new control algorithms that anticipate behavioral disturbances and improve upon the existing (deterministic) model predictive methods currently being evaluated for human-subject clinical experiments without compromising safety.

<u>Models Based on Disturbance Regimes:</u> In this work, we capture the statistical regularity of certain system disturbances, such as meals and exercise, through the notion of disturbance regimes, where in each regime we model meal or exercise events as a single-shot shock disturbance of random size. We have demonstrated the feasibility of a 24-hour closed-loop control algorithm in which the system is always preparing for the next disturbance, administering small amounts of insulin in anticipation of meal events, with more aggressive anticipatory behavior being associated with greater certainty about upcoming disturbances. Currently, we are extending the regime-based framework in the direction of "advisory" systems that provide on-demand insulin bolus recommendations to the patient. Here, the advised bolus is computed as the optimal solution to an indefinite-horizon linear quadratic problem defined by the uncertain time at which the patient will next eat.

<u>Models Based on Multiple Disturbance Function Hypotheses:</u> In this class of models, we account for correlations between behavioral events by modeling the disturbance process as a set hypothesized systematic disturbance functions representative of the patient's entire day. In prior work, we have focused on the design of an open-loop feedback control strategy based on a given set of disturbance hypotheses. Recently, we have been investigating the opportunity to generate disturbance hypotheses *automatically* by reconciling the patient's continuous monitoring data with his/her insulin pump log file. The overarching goal is to develop a method that adapts to the patient's own record of behavioral activities. In the particular case of our motivating example, this general approach will lead to a truly personalized artificial pancreas device.