# CornellEngineering

Robert Frederick Smith School of Chemical and Biomolecular Engineering



### 2020 Julian C. Smith Lectureship



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#### Monday, April 13, 2020 • 4:30pm "The Artificial Pancreas: From Engineering Research to Patient Care"

Type 1 diabetes mellitus (T1DM) is a chronic autoimmune disease affecting approximately 35 million individuals world-wide, with associated annual healthcare costs in the US estimated to be approximately \$15 billion. Current treatment requires either multiple daily insulin injections (MDI) or continuous subcutaneous insulin infusion (CSII) delivered via an insulin infusion pump. Both treatment modes necessitate frequent blood glucose measurements to determine the daily insulin requirements for maintaining near-normal blood glucose levels.

More than 30 years ago, the idea of an artificial pancreas for patients with type 1 diabetes mellitus was envisioned. The closed-loop concept consisted of an insulin syringe, a blood glucose analyzer, and a transmitter. In the ensuing years, a number of theoretical research studies were performed with computer simulations to demonstrate the relevance of advanced process control design to the artificial pancreas, with delivery algorithms ranging from simple PID, to fuzzy logic, to model predictive control. As continuous glucose sensing technology matured, including the ability to measure interstitial glucose concentrations with sufficient accuracy every 5 minutes, and the development of hardware and algorithms to communicate with and control insulin pumps, the vision of closed-loop control of blood glucose has approached a reality.

In the last 20 years, our research group has been working with medical doctors on clinical demonstrations of feedback control algorithms for the artificial pancreas. In this talk, I will outline the difficulties inherent in controlling physiological variables, the challenges with regulatory approval of such devices, and will describe several process systems engineering algorithms we have tested in clinical and outpatient settings for the artificial pancreas. I will describe our latest work in creating an embedded version of our MPC algorithm to enable a portable implementation in a medical IoT framework.

#### Tuesday, April 14, 2020 • 4:30pm "Controlling Biological Time"

A property of particular interest in systems biology is the robustness of a biophysical network: the ability to maintain some target level of behavior or performance in the presence of uncertainty and/or perturbations. For the past 20 years, our group has studied the circadian clock as a model system for closed-loop robust timekeeping. Rhythms that emerge at the gene regulatory level maintain coherence through signaling across thousands of neuronal oscillators in the hypothalamus. Synchronized behavior emerges from the networked control properties, despite the relatively "sloppy" behavior of individual components (cells).

In recent years, our attention has shifted from the analysis of natural control mechanisms in the clock to the design of "forcing" or control protocols that allow for rapid re-entrainment of the clock. Maintaining robust circadian rhythms has been linked to longevity and metabolic health. Because these rhythms are disturbed by factors such as jet lag, shift work, and high-fat diets, there is interest in developing pharmacological control strategies to modulate circadian function. The design of therapeutic strategies is currently limited by the lack of a clear mechanistic understanding of interactions between posttranslational regulators, as efficient control of clock behavior will likely require several simultaneous modulations. Although small molecules that modulate clock function might offer therapeutic approaches to such diseases, only a few compounds have been identified that selectively target core clock proteins. Using mathematical modeling and systems biology approaches, we provide a mechanistic interpretation for the relationship between candidate regulators, lending insight into circadian regulation and potential chronotherapies.

## April 13-14, 2020 • Zoom https://cornell.zoom.us/j/658909755