Dynamics and Control for the Artificial Pancreas

Healthy Regulation of Blood Glucose

The human body uses a combination of opposing manipulated variables (dual control) to achieve regulation of blood glucose using hormones produced by the pancreas, similar to a driver using the brake and gas pedals in an automobile. Insulin functions as the “brake pedal,” lowering the blood glucose by stimulating the uptake of glucose by muscle, fat, and kidney cells. The counterregulatory hormone glucagon acts primarily to break down glycogen in the liver, yielding glucose and an elevation in blood glucose levels (acting as the “gas pedal”).

Relevance of Systems and Control

The systems and control community is playing a crucial role in developing strategies for the reliable automation of blood glucose monitoring and regulation in several ways:

• Advanced control design (for example, model predictive control)
• Design of “verifiable” algorithms for regulatory approval processes
• Safety and fault analysis for medical delivery systems
• Algorithms to monitor the patient and the health of the system
• Advanced glucose calibration algorithms

Type 1 Diabetes

• Type 1 diabetes is an autoimmune disease leading to insufficient or no production of insulin by the pancreas. When untreated, the disease results in very high blood glucose levels.
• Current insulin therapies require frequent user intervention (insulin administration and blood glucose measurements). These typically open-loop methods are often ineffective in maintaining blood glucose in the normal range, resulting in large fluctuations in glucose.
• While attempting to control blood glucose intensively, hypoglycemia events (low blood sugar) frequently occur due to insulin stacking or overdosing.
• Conversely, hyperglycemia (elevated blood glucose) may lead to long-term vascular complications.
• The common insulin administration route is the subcutaneous one via either multiple daily injection (MDI) or a continuous subcutaneous insulin infusion (CSII) pump.
• Type 1 diabetes affects as many as 3 million individuals in the U.S. with associated annual medical costs of $15 billion.

The Artificial Pancreas Vision

Although type 1 diabetes is currently incurable, the development of a reliable artificial pancreas would considerably improve the lifestyle of subjects with this disease. In addition to control algorithms, an automated, fully closed-loop artificial pancreas will require sensors and actuators (see below). Recent developments in continuous blood glucose monitoring (sampling rates of approximately 1–5/min) and innovations in insulin pumps (including telemetry) are promising in this context—the enabling technologies for control engineering to make an impact are well along in development (see schematic below with devices integrated into the system).

Contributor: Francis J. Doyle III, University of California at Santa Barbara, USA
Barriers and Challenges

Several technical, policy, and cultural barriers must be addressed before a viable artificial pancreas can be developed:

- Performance metrics for closed-loop control are still a subject of discussion.
- Glucose sensor reliability and accuracy remain an issue.
- Delay in insulin action makes systems sluggish.
- Intrasubject variability is a significant challenge (for example, hour-to-hour changes in insulin sensitivity).
- Closed-loop trials must meet strict regulatory standards.

Several specific engineering challenges must also be resolved:

- Redundant arrays of glucose sensors based on different measurement methods
- Alternative insulin delivery routes, such as intraperitoneal or inhalable formulations
- Multiple-chamber pumps that will allow delivery of insulin and/or glucagon and amylin
- Personalization and dynamic predictive modeling of individual patients
- Communication and interfacing standards for the artificial pancreas
- Well-defined, clinically oriented benchmark scenarios to evaluate control design
- Faster-acting insulin formulations

The Artificial Pancreas System and Preliminary Closed-Loop Trials

Intensive research is under way in all facets of the artificial pancreas. Multiple control strategies are being explored in human clinical studies around the world with good initial results. As demonstrated, safe glucose regulation, minimizing hyperglycemia, and overcoming meal disturbances are being evaluated in human clinical studies. A recent milestone has been the development of the Artificial Pancreas System (APS©) platform at the University of California at Santa Barbara in collaboration with the Sansum Diabetes Research Institute. It is also being used to link glucose sensors and insulin pumps using wireless protocols. The APS© platform provides a flexible mechanism for integrating hardware (such as glucose sensors and insulin pumps, in addition to computational devices), software algorithms, and human-machine interfaces (see top figure at right).

The APS© is being used in closed-loop trials around the world to test the efficacy of a variety of algorithms for blood glucose control as well as other advanced control applications. Several clinical trials using zone model predictive control with unannounced meals and exercise have been performed at the Sansum Diabetes Research Institute with good results (see bottom figure at right).