Novel Insulin Delivery Profiles for Mixed Meals in Basal-Bolus and Closed-Loop Artificial Pancreas Therapy for Type 1 Diabetes Mellitus

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Diabetes mellitus is a chronic condition caused either by the inability of the pancreas to produce enough insulin or insufficient insulin secretion accompanied by the body's resistance to the effects of insulin. The former is known as type 1 diabetes mellitus, which forms the subject matter of this study. It most often occurs in children and adolescents, affecting approximately 34 million people worldwide. Without adequate insulin secretion, the body is unable to metabolize blood glucose and use it as an efficient source of energy. Since glucose is one of the main energy sources for most cells in the body, a stable blood glucose concentration is essential to avoid serious complications that could potentially lead to death. Too high glucose concentrations (hyperglycemia) may cause blindness, nerve damage, and kidney failure, whereas too low concentrations (hypoglycemia) can result in seizures, unconsciousness, and weakness. Hence, people with type 1 diabetes require insulin therapy to maintain normal blood glucose concentrations.

Rapid increases in blood glucose concentration following meals (postprandial) are difficult to control in people with type 1 diabetes due to the lack of endogenous insulin production. As a result, meal compensation is one of the most important and challenging aspects of diabetes treatment. Major available treatment modes for type 1 diabetes include multiple daily injections of insulin and insulin pump therapy that provides continuous subcutaneous insulin infusion. These are known as open-loop methods since they rely primarily on user inputs and not glucose measurements. Automated closed-loop insulin delivery, also referred to as the artificial pancreas, is an emerging treatment approach aimed at eliminating the need for user inputs [1]. The system combines a glucose sensor, insulin infusion pump, and a controller that regulates the insulin infusion based on glucose measurements from the sensor. Available therapy offers only limited insulin dosing (bolus) options that cannot provide optimal postprandial control for all types of meals.

The present work aims at finding optimal insulin delivery profiles for a variety of meal compositions through simulation trials on ten adult subjects [2]. The main purpose is to improve open- and closed-loop insulin therapy by constructing an insulin regimen library with a set of appropriate insulin delivery recommendations for meals with varied glucose absorption rates. The simulation results show that the optimal insulin delivery profiles for low-fat meals are either a momentary insulin dose (normal bolus) or infusion over a shorter time period (insulin wave). Interestingly, the optimal open-loop regimens for high-fat meals typically comprise two

consecutive insulin waves, but can extend to multiple waves for large slow absorbing meals. Preliminary investigations of the optimal closed-loop regimens also display bi- or triphasic patterns for high-fat meals.

The novel insulin delivery profiles identified in this work comprise new and unique waveforms that have demonstrated better postprandial glucose control than existing schemes in simulated trials. Overall, the proposed closed-loop strategy shows superior performance and is a realistic approach that could have real-life applications in an artificial pancreas for people with type 1 diabetes mellitus.

References

[1] Cobelli, C., Renard, E., Kovatchev, B. (2011). Artificial Pancreas: Past, Present, Future. *Diabetes*, *60*, 2672-2682.

[2] Srinivasan, A. (2013). *Novel Insulin Delivery Algorithms for Mixed Meals in Basal-Bolus and Closed-Loop Artificial Pancreas Therapy for Type 1 Diabetes Mellitus*. Master's Thesis, Department of Automatic Control, Lund University.